CODEXIS INC
Form 10-K
March 01, 2019

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K
(Mark One)
ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2018
¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to .
Commission File No.: 001-34705

Codexis, Inc.
(Exact name of Registrant as specified in its charter)

Delaware	71-0872999
(State or other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
200 Penobscot Drive, Redwood City, California	94063
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: (650) 421-8100
Securities Registered Pursuant to Section 12(b) of the Act:

Title of Each Class:	Name of Each Exchange on which Registered:
Common Stock, par value $0.0001 per share	The Nasdaq Global Select Market

Securities Registered Pursuant to Section 12(g) of the Act: None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No ý
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No ý
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No ¨
Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ý No ¨
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ý
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See the definitions of "large accelerated filer," "accelerated

filer" and "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer ý	Accelerated filer ¨
Non-accelerated filer ¨	Smaller reporting company ¨
	Emerging growth company ¨

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No ý

The aggregate market value of voting common stock held by non-affiliates of Codexis as of June 30, 2018 was approximately $731.5 million based upon the closing price reported for such date on the Nasdaq Global Select Market.

As of February 22, 2019, there were 54,158,617 shares of the registrant's Common Stock, par value $0.0001 per share, outstanding.

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DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement to be filed with the Commission pursuant to Regulation 14A in connection with the registrant's 2019 Annual Meeting of Stockholders, to be filed subsequent to the date hereof, are incorporated by reference into Part III of this Report. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission not later than 120 days after the conclusion of the registrant's fiscal year ended December 31, 2018. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

The following discussion and analysis should be read in conjunction with our audited consolidated financial statements and the related notes that appear elsewhere in this Annual Report on Form 10-K. This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended ("the Exchange Act"), particularly in Part I, Item 1: "Business," Part I, Item 1A: "Risk Factors" and Part 2, Item 7: "Management's Discussion and Analysis of Financial Condition and Results of Operations." These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "e or "continue," and similar expressions or variations. All statements other than statements of historical fact could be deemed forward-looking, including, but not limited to: any projections of financial information; any statements about historical results that may suggest trends for our business; any statements of the plans, strategies, and objectives of management for future operations; any statements of expectation or belief regarding future events, technology developments, our products, product sales, expenses, liquidity, cash flow, market growth rates or enforceability of our intellectual property rights and related litigation expenses; and any statements of assumptions underlying any of the foregoing. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Accordingly, we caution you not to place undue reliance on these statements. For a discussion of some of the factors that could cause actual results to differ materially from our forward-looking statements, see the discussion on risk factors that appear in Part I, Item 1A: "Risk Factors" of this Annual Report on Form 10-K and other risks and uncertainties detailed in this and our other reports and filings with the Securities and Exchange Commission ("SEC"). The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

PART I

ITEM 1. BUSINESS

COMPANY OVERVIEW

We discover, develop and sell proteins that deliver value to our clients in a growing set of industries. We view proteins as a vast untapped source of value-creating materials, and we are using our proven technologies, which we have been continuously improving over our sixteen-year history, to commercialize an increasing number of novel proteins, both as proprietary Codexis products and in partnership with our customers.

We are a pioneer in the harnessing of computational technologies to drive biology advancements. Since our inception in 2002, we have made substantial investments in the development of our CodeEvolver® protein engineering technology platform, the primary source of our competitive advantage. Our technology platform is powered by proprietary, artificial intelligence-based, computational algorithms that rapidly mine our large and continuously growing library of protein variants' performance attributes. These computational outputs enable increasingly reliable predictions for next generation protein variants to be engineered, enabling delivery of targeted performance enhancements in a time-efficient manner. In addition to its computational prowess, our CodeEvolver® protein engineering technology platform integrates additional modular competencies, including robotic high-throughput screening and genomic sequencing, organic chemistry and process development, which are all coordinated to create our novel protein innovations.

Our approach to developing commercially viable biocatalytic manufacturing processes begins by conceptually designing the most cost-effective and practical process for a targeted product. We then develop optimized protein catalysts to enable that process design using our CodeEvolver® protein engineering platform technology. Engineered protein catalyst candidates - many thousands for each protein engineering project - are then rapidly screened and validated in high throughput screening under relevant manufacturing operating conditions. This approach results in an optimized protein catalyst enabling cost-efficient processes that typically are relatively simple to run in conventional manufacturing equipment. This also allows for the efficient technical transfer of our process to our manufacturing partners.

The successful embodiment of our CodeEvolver® protein engineering technology platform in commercial manufacturing processes requires well-integrated expertise in a number of technical disciplines. In addition to those directly involved in practicing our CodeEvolver® protein engineering platform technology, such as molecular biology, enzymology, microbiology, cellular engineering, metabolic engineering, bioinformatics, biochemistry and high throughput analytical chemistry, our process development projects also involve integrated expertise in organic chemistry, chemical process development, chemical engineering, fermentation process development and fermentation engineering. Our integrated, multi-disciplinary approach to biocatalyst and process development is a critical success factor for our company.

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the pharmaceuticals market, which remains our primary business focus. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development.

We have also used the technology to develop protein catalysts for use in the fine chemicals market. The fine chemicals market consists of several large market verticals, including food and food ingredients, animal feed, flavors, fragrances and agricultural chemicals.

We have also begun using the CodeEvolver® protein engineering technology platform to develop early stage, novel biotherapeutic product candidates, both for our customers and for our own business, most notably our lead program for the potential treatment of phenylketonuria ("PKU") in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we entered into a Global Development, Option and License Agreement (the "Nestlé Agreement") with Nestec Ltd. ("Nestlé Health Science") to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license to develop and commercialize CDX-6114.

In April 2018, we entered into a strategic agreement (the "Porton Agreement") with Porton Pharma Solutions, Ltd. ("Porton") to license key elements of our platform technology to Porton’s global custom intermediate and active pharmaceutical ingredients ("API") development and manufacturing business. This gives us access to a wide variety of small and medium-sized pharmaceutical customers.

We are also using our technology to develop enzymes for customers using next generation sequencing ("NGS") and polymerase chain reaction ("PCR/qPCR") for in vitro molecular diagnostic and genomic research applications. Our first enzyme is a ligase which we began marketing to customers in 2018.

BUSINESS SEGMENTS

We manage our business as two business segments: Performance Enzymes and Novel Biotherapeutics. See Note 15, "Segment, Geographical and Other Revenue Information" in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Performance Enzymes

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the pharmaceuticals market, and to date this continues to be our largest market served. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. We have also used the technology to develop customized enzymes for use in other industrial markets. These markets consist of several large industrial verticals, including food and food ingredients, animal feed, flavors, fragrances, and agricultural chemicals. We also use our technology to develop enzymes for customers using NGS and PCR/qPCR for in vitro molecular diagnostic and molecular biology research applications. In April 2018, we entered into the Porton Agreement related to our strategic collaboration with Porton to license key elements of our world-leading biocatalyst technology for use in Porton's global custom intermediate and API development and manufacturing business.

Novel Biotherapeutics

We are also targeting new opportunities in the pharmaceutical industry to discover, improve, and/or develop biotherapeutic drug candidates. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity. Most notable is our lead program for the potential treatment of hyperphenylalaninemia ("HPA") (also referred to as PKU) in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we announced a strategic collaboration with Nestlé Health Science to advance CDX-6114, our own novel orally administrable enzyme therapeutic candidate for the potential treatment of PKU. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, which was conducted in Australia. In November 2018, we announced top-line results from the Phase 1a study in healthy volunteers with CDX-6114. In December 2018, Nestlé Health Science became obligated to pay us an additional $1.0 million within 60 days after the achievement of a milestone relating to formulation of CDX-6114. In January 2019, we received notice from the U.S. Food and Drug Administration (the "FDA") that it had completed its review of our investigational new drug application ("IND") for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, Nestlé Health Science is obligated to pay us $3.0 million within 60 days after exercise of the option. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, "Subsequent Events" in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details.

We have also developed a pipeline of other biotherapeutic drug candidates in which we expect to continue to make additional investments with the aim of advancing additional product candidates targeting other therapeutic areas.

OUR STRATEGY

Our strategy is to grow our revenues, profits, and stockholder value by leveraging our CodeEvolver® protein engineering technology platform in the following ways:

- Licensing our CodeEvolver® protein engineering technology platform. We intend to continue to pursue opportunities to license our CodeEvolver® protein engineering technology platform to third parties so they can create cost-saving protein catalyst solutions utilizing their own in-house protein engineering capability.
- Growing our pharmaceutical protein catalysts business. We intend to continue to pursue opportunities in the pharmaceutical market to use our protein catalysis products and services to reduce the costs for manufacturing small

molecule drugs. We intend to increase the number of pharmaceutical customers and processes that utilize and benefit from our novel, cost-saving protein catalyst solutions.

- Creating and advancing novel biotherapeutic drug candidates. We intend to continue to pursue opportunities to apply our protein engineering capabilities to the creation and development of novel biotherapeutic drug candidates, both in partnership with customers and as proprietary Codexis drug candidates. We have also invested in research and development in an effort to generate additional early stage novel biotherapeutic candidates.
- Growing our fine chemicals protein catalysts business. We intend to continue to pursue opportunities in the fine chemicals market to use protein catalysis products and services to reduce the costs for manufacturing in adjacent markets like food and food ingredients. We intend to increase the number of fine chemical customers and processes who utilize and benefit from our novel, cost-saving protein catalyst solutions.
- Developing high-performance enzymes for use in diagnostic applications. We intend to offer high-performance enzymes to customers using NGS and PCR/qPCR for in vitro molecular diagnostic applications.

In this Annual Report, the “Company,” “we,” “us” and “our” refer to Codexis, Inc. and its subsidiaries on a consolidated basis.

OUR MARKET OPPORTUNITIES

Pharmaceutical Market

We believe the pharmaceutical industry represents a significant market opportunity for us and is our primary business focus. Pharmaceutical companies are in constant search for new drugs to offer to their customers, and are under significant competitive pressure both to reduce costs and to increase the speed to market for their products. To meet these pressures, pharmaceutical companies are discovering and developing novel protein-based drug products, as well as seeking manufacturing processes for their new and existing drugs that reduce overall costs, simplify production and increase efficiency and product yield, while not affecting drug safety and efficacy. Cost reduction is even more important to developers (known as innovators) of patent-protected pharmaceutical products when the patents for those products expire and such innovators are forced to compete with manufacturers of generic drugs.

The pharmaceutical product lifecycle begins with the discovery of new chemical entities and continues through preclinical and clinical development, regulatory review and approval, commercial scale-up, product launch, and, ultimately, patent expiration and the transition from branded to generic products. As innovators develop, produce and then market products, manufacturing priorities and processes evolve. Historically, innovators have focused on production cost reduction in the later stages of clinical development and have been reluctant to make process changes after a product has been launched. However, as pressures to reduce costs have increased, innovators have pursued cost reduction measures much earlier in the pharmaceutical product lifecycle and are increasingly looking for opportunities to improve their operating margins, including making manufacturing process changes for marketed products after the products have been launched if these changes can result in significant cost reductions. As a result, innovators are investing in new technologies, including our CodeEvolver® protein engineering technology platform, to improve their manufacturing productivity and efficiency or outsourcing the manufacture of their intermediates and APIs.

Our Solutions for the Pharmaceutical Market

Small Molecule Manufacturing Cost Reduction

Our pharmaceutical customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. Our CodeEvolver® protein engineering technology platform enables us to deliver solutions to our customers in this market by developing and delivering optimized protein catalysts that perform chemical transformations at a lower cost and improve the efficiency and productivity of manufacturing processes. We provide value throughout the pharmaceutical product lifecycle. Our products and services allow us to provide benefits to our pharmaceutical customers in a number of cost saving ways, including any - and sometimes all - of the following:

- reducing the use of raw materials and reagents;
- eliminating multiple steps in the manufacturing process;
- improving purity, productivity and yield;
- using water as a primary solvent;
- eliminating hazardous inputs;
- enabling the use of simple equipment and reducing the need for capital expenditure;

•reducing energy requirements;

•reducing the generation of chemical byproducts or waste; and
•reducing the need for late-stage purifications.

Early in a pharmaceutical product's lifecycle, pharmaceutical manufacturers can use our protein catalyst products and services to reduce manufacturing costs. If an innovator incorporates our products or processes into an approved product, we expect the innovator to continue to use our products or processes at least over the patent life of the marketed drug.

Pharmaceutical manufacturers can also use our products and services to reduce manufacturing costs after a product is launched. At this stage, changes in the manufacturing process originally approved by the drug regulator may require additional regulatory review. Typically, pharmaceutical companies will only seek regulatory approval for a manufacturing change if substantial cost savings are realizable. We believe that the cost savings associated with our products may lead our customers to change their manufacturing processes for approved products and, if necessary, seek regulatory approval of the new processes which incorporate our proteins. Moreover, we believe these cost savings are attractive to generics manufacturers, who compete primarily on price.

In addition, manufacturing processes that utilize our protein catalysts can frequently enable processes that are more sustainable and environmentally friendly compared to alternative, traditional manufacturing approaches. This has led us to earn three U.S. EPA Presidential Green Chemistry Challenge awards for improved pharmaceutical manufacturing processes since we were founded. All three of these awards were associated with blockbuster drug products.

Discovery and Development of Biotherapeutic Drug Candidates

We are also targeting new opportunities in the pharmaceutical industry to discover or improve biotherapeutic drug candidates for our customers. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity.

We approach biopharmaceutical companies to collaborate and utilize our platform technology for the discovery of specific novel biotherapeutic candidates. We currently have one such biotherapeutic discovery partnership in progress under the strategic collaboration agreement with Nestlé Health Science. We continue to pursue other customers who could benefit by applying our CodeEvolver® protein engineering platform technology to improve the discovery and/or development of other biotherapeutics in partnership with us.

Biotherapeutic Product Discovery and Development

We are also using our platform technology to self-fund the development of our own early stage, novel enzyme therapeutic product candidates. The lead product candidate is CDX-6114, an enzyme which we have engineered to be orally administered and is being developed as a potential treatment of PKU in humans. PKU is an inborn metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. As a result, phenylalanine accumulates to toxic levels in the brain, causing serious neurological problems including intellectual disability, seizures and cognitive and behavioral problems. To avoid toxic levels of phenylalanine in their blood, individuals with PKU must follow a strict, life-long diet that is low in phenylalanine and supplement their diet with a synthetic phenylalanine-free formula to provide them with sufficient nutrients. Maintaining a strict, life-long diet can be challenging for individuals with PKU. There are an estimated 50,000 people with PKU in the developed world.

In addition to the PKU program, we have focused our self-funded biotherapeutic investments with aim to discover therapeutic solutions for four additional rare disease conditions. Two of those programs are targeting potential enzyme replacement treatments for patients with inborn errors of amino acid metabolism diseases. The other two programs are targeting potential treatments for patients with lysosomal storage diseases. We expect to continue to make additional investments with the aim of generating additional product candidates targeting these, and potentially other therapeutic areas.

Nestlé Health Science

On October 12, 2017 (the "Effective Date"), we entered into a Global Development, Option and License Agreement (the "Nestlé Agreement") with Nestlé Health Science and, solely for the purpose of the integration and the dispute resolution clauses of the Nestlé Agreement, Nestlé Health Science S.A., pursuant to which we granted to Nestlé Health Science, under certain of our patent rights and know-how: (i) an option to obtain an exclusive, worldwide, royalty-bearing, sublicenseable license to develop and commercialize certain products (each, a "Product") based on CDX-6114 and our other therapeutic enzyme product candidates covered by specified patent applications for the treatment of hyperphenylalaninemia ("HPA"), and (ii) an exclusive right of first negotiation (the "Right of First Negotiation") for a period of five years to obtain an exclusive worldwide license to develop and commercialize up to two enzymes discovered by us for use in the field of the prevention, diagnosis, treatment and

management of inborn errors of amino acid metabolism. We are not under any obligation to undertake any research and development activities relating to inborn errors of amino acid metabolism. HPA (also referred to as PKU) is a medical condition characterized by elevated concentrations of the amino acid phenylalanine in the blood. PKU can result in severe HPA.

In February 2019, Nestlé Health Science exercised its option to receive an exclusive license to further develop and commercialize CDX-6114 and our other therapeutic enzyme product candidates covered by specified patent applications for the treatment of PKU (each, a "Compound"). Under the terms of the Nestlé Agreement, upon option exercise, Nestlé Health Science received a license to the Compound, other than any enzyme that has other clinically significant, specified activity against another molecule, unless that enzyme's specified activity against phenylalanine is ten times greater than its activity against such other molecule (in which case it is not excluded). Furthermore, we generally will retain the right to use any enzyme as a biocatalyst, provided that preclinical development of such enzyme has not commenced. The first Compound to be developed under the Nestlé Agreement was our enzyme CDX-6114.

The Nestlé Agreement also sets forth the parties' respective obligations for development, commercialization, regulatory and manufacturing and supply activities for CDX-6114 and Product containing CDX-6114. Prior to Nestlé Health Science exercising its option to receive an exclusive license to CDX-6114, we were generally responsible for development activities, including conducting a Phase 1a clinical study. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. Our development activities were governed by a development plan and overseen by a joint steering committee. The parties established a patent committee to discuss strategies and coordinate activities for the patents related to CDX-6114 and Product containing CDX-6114, and we will jointly own all inventions and information that result from each party's activities performed under the Nestlé Agreement. The Nestlé Agreement also contains customary representations and warranties by the parties, intellectual property protection provisions, certain indemnification rights in favor of each party and customary confidentiality provisions and limitations of liability.

Nestlé Health Science paid us an upfront cash payment of $14.0 million in the fourth quarter of 2017. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114 which was conducted in Australia. In November 2018, we announced top-line results from the Phase 1a study in healthy volunteers with CDX-6114. In January 2019, we received notice from the U.S. Food and Drug Administration (the "FDA") that it had completed its review of our investigational new drug application ("IND") for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license for the global development and commercialization of CDX-6114 for the management of PKU. The exercise of the option triggers a $3 million milestone payment. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, "Subsequent Events" in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details.

Other potential payments from Nestlé Health Science to us under the Agreement include (i) development and approval milestones of up to $86.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of products containing an enzyme covered by the agreement as its sole active ingredient.

In addition to the Nestlé Agreement, we and Nestlé Health Science concurrently entered into a strategic collaboration agreement pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® platform technology to develop novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas.

Fine Chemicals and Industrial Enzyme Markets

Beyond the pharmaceutical industry, our CodeEvolver® protein engineering platform technology has enabled cost-savings for our partners in the fine chemicals markets, and the food industry in particular. In November 2016, we entered into an exclusive agreement with Tate & Lyle, a market-leading food ingredients company, to supply a proprietary enzyme for use in Tate & Lyle's food ingredient production. In March 2017, we announced a second multi-year research and development services agreement with Tate & Lyle for the development of a second ingredient for the food ingredient industry. We engineered a suite of enzymes that enable Tate & Lyle's novel bioconversion route for the manufacture of their newly-launched zero-calorie TASTEVA® M Stevia sweetener.

We are seeking to expand our enzyme offerings in the fine chemical and industrial enzyme markets within and beyond the food industry, including, for example, to the animal feed, agricultural chemicals and flavors and fragrances markets.

Molecular Biology and In Vitro Diagnostic Enzymes

We believe that our Codexis protein engineering capability can also be deployed to commercialize novel enzymes as improvements to enzymes consumed by customers in many industrial sectors. As our first effort in this strategy, we have developed an enzyme for customers using NGS and PCR/qPCR for in vitro molecular diagnostic applications. Our first proprietary enzyme for this market targets improved library preparation for NGS users and is currently being beta tested. We are also currently working on a second enzyme, a DNA polymerase, which is being prepared for beta testing.

Licensing Our CodeEvolver® Protein Engineering Technology Platform

Our CodeEvolver® protein engineering technology platform enables rapid development of custom-designed enzymes that are highly optimized for efficient manufacturing processes. We intend to continue to enter into license arrangements with third parties that will allow them to use our CodeEvolver® protein engineering technology platform to discover and develop novel proteins for their internal use. To date, we have entered into platform technology licensing agreements with each of GlaxoSmithKline and Merck.

GlaxoSmithKline

We entered into our first CodeEvolver® protein engineering Platform Technology Transfer, Collaboration and License Agreement ("GSK CodeEvolver® Agreement") on July 10, 2014 with GlaxoSmithKline Intellectual Property Development Limited, a subsidiary of GlaxoSmithKline plc (collectively, "GSK"), pursuant to which we granted GSK a non-exclusive, worldwide license to use our CodeEvolver® protein engineering technology platform in the field of human healthcare for its internal development purposes.

Under the GSK CodeEvolver® Agreement, we transferred our CodeEvolver® protein engineering technology platform to GSK over a twenty-one-month period that began on July 10, 2014. As a part of this technology transfer, we provided to GSK our proprietary enzymes, proprietary protein engineering protocols and methods, and proprietary software algorithms. In addition, teams of our and GSK scientists participated in technology training sessions and collaborative research projects at our laboratories in Redwood City, California and at GSK's laboratories in Upper Merion, Pennsylvania. The technology transfer was completed in April 2016 and our CodeEvolver® protein engineering technology platform has been installed at GSK's Upper Merion, Pennsylvania site. We have the potential to receive additional contingent payments that range from $5.75 million to $38.5 million per project based on GSK's successful application of the licensed technology.

We are also eligible to receive royalties based on net sales, if any, of a limited set of products developed by GSK using the CodeEvolver® protein engineering technology platform.

The licenses to GSK were granted under certain patents, patent applications and know-how that we owned or controlled as of the effective date of the GSK CodeEvolver® Agreement and that cover our CodeEvolver® protein engineering technology platform and certain enzymes useful in the Field. Any improvements to our CodeEvolver® protein engineering technology platform during the technology transfer period were included in the license grants from us to GSK.

Under the GSK CodeEvolver® Agreement, GSK owns (the "GSK-Owned Technology") (a) any enzyme technology that was developed during a project under the GSK CodeEvolver® Agreement that used our CodeEvolver® protein engineering technology platform during the technology transfer period and (b) the methods of use of any Project Enzyme in compound synthesis that were developed during the technology transfer period. GSK granted to us a worldwide, non-exclusive, fully paid-up, royalty-free license, with the right to grant sublicenses, to use outside of the GSK Exclusive Field, the GSK-Owned Technology that was developed during the technology transfer period.

Until July 10, 2019 (the "Embargo Period"), GSK is prohibited from using the CodeEvolver® protein engineering technology platform for the use, research or development (whether in vitro or in vivo) or commercialization of any enzyme or enzyme fusion protein that (a) effects a chemical transformation in humans or (b) facilitates, assists, transports or enables the action, dispersion, absorption or bioavailability of a molecule, biologic agent, drug product, therapeutic agent or other compound in humans (the "Embargo Field"). GSK is permitted to use our CodeEvolver® protein engineering technology platform during the Embargo Period to develop and use an enzyme or enzyme fusion protein that (x) is used by GSK solely as a research reagent or a research tool within the Embargo Field, (y) is used to synthesize a small-molecule compound owned or controlled by GSK or (z) facilitates, assists, transports or enables the

action, dispersion, absorption or bioavailability of a small-molecule compound that is owned or controlled by GSK. The term of the GSK CodeEvolver® Agreement continues, unless earlier terminated, until the expiration of all payment obligations under the GSK CodeEvolver® Agreement. GSK can terminate the GSK CodeEvolver® Agreement by providing 90 days written notice to us.

Merck

On August 3, 2015, we entered into a CodeEvolver® platform technology transfer and license agreement (the "Merck CodeEvolver® Agreement") with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. (collectively, "Merck").

The Merck CodeEvolver® Agreement allows Merck to use our proprietary CodeEvolver® protein engineering platform technology in the field of human and animal healthcare.

Under the terms of the Merck CodeEvolver® Agreement, we granted to Merck a non-exclusive worldwide license to use the CodeEvolver® protein engineering technology platform to research, develop and manufacture novel enzymes for use by Merck in its internal research programs ("Merck Non-Exclusive Field"). The license to Merck is exclusive for the research, development and manufacture of novel enzymes for use by Merck in the chemical synthesis of therapeutic products owned or controlled by Merck ("Merck Exclusive Field"). Merck has the right to grant sublicenses to affiliates of Merck and, in certain limited circumstances, to third parties. We also granted to Merck a license to make or have made products manufactured using the CodeEvolver® protein engineering technology platform with a right to grant sublicenses solely to affiliates of Merck, contract manufacturing organizations and contract research organizations. The manufacturing license is exclusive in the Merck Exclusive Field and non-exclusive in the Merck Non-Exclusive Field. The licenses are subject to certain limitations based on pre-existing contractual obligations that apply to the technology and intellectual property that are the subject of the license grants. The licenses do not permit the use of the CodeEvolver® protein engineering technology platform to discover any therapeutic enzyme, diagnostic product or vaccine. In addition, Merck is prohibited from using the CodeEvolver® protein engineering technology platform to develop or produce enzymes or any other compounds for or on behalf of any third parties except in a very limited manner when Merck divests a therapeutic product that is manufactured using an enzyme developed using the CodeEvolver® protein engineering technology platform.

Under the terms of the Merck CodeEvolver® Agreement, Merck paid us $18.0 million comprised of up-front technology transfer and license fees and milestone payments over the technology transfer period of 15 months from August 3, 2015, the effective date of the Merck CodeEvolver® Agreement. We also have the potential to receive product-related payments of up to $15.0 million for each API that is manufactured by Merck using one or more enzymes that have been developed or are in development using the CodeEvolver® protein engineering technology platform during the 10-year period that begins on the conclusion of the 15-month technology transfer period. These product-related payments, if any, will be paid by Merck to us for each quarter that Merck manufactures API using a CodeEvolver®-developed enzyme. The payments will be based on the total volume of API produced using the CodeEvolver®-developed enzyme. We have the right to conduct an annual audit to confirm that all payments that are owed to us have been paid in full and on time.

Under the Merck CodeEvolver® Agreement, we transferred the CodeEvolver® protein engineering technology platform to Merck over the period from August 2015 through September 2016. As part of this technology transfer, we provided to Merck our proprietary enzymes, proprietary protein engineering protocols and methods, and proprietary software algorithms. We provided additional enzyme evolution services to Merck at our laboratories in Redwood City through November 2016. The remaining deferred revenue relating to the upfront payment was recognized upon completion of the additional enzyme evolution services.

The licenses to Merck are granted under patents, patent applications and know-how that we owned or controlled as of the effective date of the Merck CodeEvolver® Agreement and that cover the CodeEvolver® protein engineering technology platform. Any improvements to the CodeEvolver® protein engineering technology platform during the technology transfer period are also included in the license grants from Codexis to Merck. Following the technology transfer period, Merck can exercise annual options that, upon payment of certain option fees, would extend Merck's license to include certain improvements to the CodeEvolver® protein engineering technology platform that arise during the three-year period that begins at the end of the technology transfer period.

Under the Merck CodeEvolver® Agreement, we own any improvements to our protein engineering methods, processes and algorithms that arose and any enzyme technology or process technology that are developed during an evolution program or additional services. Merck owns (the "Merck-Owned Technology") (a) any enzyme technology that is developed solely by Merck under the Merck CodeEvolver® Agreement using the CodeEvolver® protein engineering

technology platform (a “Project Enzyme”) and (b) the methods of use of any Project Enzyme or any enzyme developed jointly by Merck and us using the CodeEvolver® protein engineering technology platform. Merck granted to us a worldwide, non-exclusive, fully paid-up, royalty-free license, with the right to grant sublicenses, to use the Merck-Owned Technology outside of the Merck Exclusive Field.

For each API that Merck manufactures using an enzyme developed with the CodeEvolver® protein engineering technology platform, we will have a right of first refusal to supply Merck with the enzyme used to manufacture the API if Merck outsources the supply of the enzyme. Our right of first refusal applies during the period that begins on the completion of a phase III clinical trial for the product containing the API and ends five years following regulatory approval for such product.

The Merck CodeEvolver® Agreement has a term that continues, unless earlier terminated, until the expiration of all payment obligations under the agreement. Merck may terminate the Merck CodeEvolver® Agreement by providing 90 days written notice to us. We can terminate the Merck CodeEvolver® Agreement by providing 30 days written notice to Merck if we determine, pursuant to our contractual audit rights under the Merck CodeEvolver® Agreement, that Merck has repeatedly failed to make required payments to us and/or materially underpaid us an amount due under the Merck CodeEvolver® Agreement. In the event the Merck CodeEvolver® Agreement is terminated earlier by Merck, or by us due to an uncured material breach by Merck, or if Merck sells or transfers to a third party any Merck business or facility that includes any of our proprietary materials, information or technology, we have the right to conduct an audit of Merck's facilities to confirm that all of our proprietary materials, information and technology have been destroyed. The Merck CodeEvolver® Agreement contains indemnification provisions under which Merck and we have agreed to indemnify each other against certain third party claims.

In September 2016, we completed the full transfer of the engineering platform technology and earned milestone revenue of $8.0 million. We received the $8.0 million milestone payment in the fourth quarter of 2016. In October 2018, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we amended certain licensing provisions and one exhibit. In January 2019, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we will install certain CodeEvolver® protein engineering technology upgrades into Merck's platform license installation and maintain those upgrades for a multi-year term.

Protein Catalyst Products and Services

Our protein catalyst products and services can deliver value to our customers in multiple potential ways:

- manufacture their products at lower cost;
- manufacture their products with lower fixed capital investment;
- reduce the cost of development of complex chemical synthesis processes;
- enable their products to achieve higher product purity;
- reduce the risk of adverse effects arising from product impurities;
- allow the removal of entire steps from chemical production; and
- provide flexibility to apply at any point across their product's lifecycle.

Our products include protein catalysts, chemical intermediates and Codex® Biocatalyst Panels and Kits. We sell our products worldwide primarily through our direct sales and business development force in the United States and Europe.

In addition to products, we also offer research and development services to our customers. These research and development service agreements often contain service fee payments and intellectual property provisions under which we screen and/or engineer protein catalysts for customers in connection with their process development efforts. In these collaborations, we typically receive consideration in the form of one or more of the following: up-front payments, milestone payments, payments for screening and engineering services, licensing fees and royalties.

Protein Catalysts

We often sell protein catalysts (also referred to as biocatalysts or enzymes), by the gram or kilogram, that have already been engineered, scaled up, and installed in a customer's commercial process. For example, we sell protein catalysts to Merck for their manufacture of Sitagliptin, the active ingredient in Januvia®. We also sell protein catalysts which are in developmental stages. These are enzymes that are sold in batches or by the gram or kilogram that are in the process of being engineered or scaled up by Codexis, or are in the process of being trialed or approved for use in the customer's process. We may sell batches of specific protein catalysts that are in the middle of our protein engineering efforts to test their performance at a larger customer scale. We also may sell batches of specific protein catalysts for use in a customer's developmental products (for example, to trial in a customer's Phase II drug candidate process). Finally, we may sell batches of specific protein catalysts as a customer performs trials for approval in their

commercial manufacturing operations.

Chemical Intermediates

In some cases, we sell intermediate chemicals products that are produced in a process that uses our protein catalysts. These chemical intermediates are then used by our customer for further chemical processing.

Codex® Biocatalyst Panels and Kits

We sell kits and panels of our protein catalysts. These kits and panels assemble a relevant subset of our engineered enzymes to enable customers to perform chemistry screening on their own. These kits and panels are organized by specific types of chemical reactions that are widely applicable in the pharmaceutical and fine chemical markets.

Protein Catalyst Screening Services

If a customer prefers, rather than purchasing our Codex® Biocatalyst Panels or Kits to use for its own screening, it may send us its starting materials and desired chemical reaction, and we will test against our existing libraries of enzymes on a research and development service fee basis. If we detect desired activity in a specific enzyme, we can supply the customer with this enzyme or perform engineering services to improve the performance of the enzyme.

Protein Engineering Services

We work with our customers throughout their product development lifecycle to optimize enzymes that have been engineered specifically to perform a desired process according to a highly selective set of specifications. We typically charge customers for research and development services by project or project-month. These are typically larger research and development service fees than screening services.

The protein engineering process starts by identifying genes that code for enzymes known to have the general type of catalytic reactivity for a desired chemical reaction. Typically, we identify gene sequences from our extensive in-house collection or from published databases and then synthesize candidate genes having those sequences. Using a variety of biotechnology tools, we diversify these genes by introducing mutations, giving rise to changes in the enzymes for which they encode. The methods for diversifying these genes, and types of diversity being tested, often vary over the course of a protein engineering program. For finding initial diversity, methods typically include random mutagenesis and site-directed (included computational structure-guided) mutagenesis. We also test mutational variations from related enzymes found in different organisms.

Once we have identified potentially beneficial mutations, we create libraries of thousands of variants with combinations of these mutations. With our proprietary genetic manipulation tools, we generate libraries of genes that have programmed and random combinations of the mutations for testing. The pool of genes is used to transform host cells, which entails introducing the various genes into host cells. These cells are then grown into colonies. Cells from individual colonies are cultured in high throughput to produce the enzyme encoded by the genetic variant in those cells. The enzymes expressed by these cells are then screened in high throughput using test conditions relevant to the desired process. The screening results allow us to identify and catalog individual genes that produce improved enzymes with beneficial mutations as well as enzymes having detrimental ones. Using specifically developed test conditions and analytical methods, we can identify variant enzymes that exhibit various improved performance characteristics, such as stability, activity and selectivity, under conditions relevant to the desired chemical process.

In the next step in our optimization process, we use our proprietary bioinformatics software to analyze protein sequence-activity relationships. Our software and algorithms relate the screening results to the mutations and rank the individual and interacting protein sequence mutations with regard to their degree of benefit or detriment, relative to the process parameter(s) tested. Using this information, we can create a select pool of mutational diversity in the next iteration to further the accumulation of beneficial diversity and cancel out detrimental diversity in the individual genes in the resulting library. The gene that codes for the best performing enzyme in one iteration is used as the starting gene for the next iteration of recombination and screening. As the enzymes improve over these iterations, the screening conditions are made increasingly more stringent. In this way, the protein catalyst is rapidly optimized until all in-process performance requirements have been achieved and the economic objectives for the desired process have been met.

INTELLECTUAL PROPERTY

Our success depends in large part on our ability to protect our proprietary products and technology under patent, copyright, trademark and trade secret laws. We also rely heavily on confidential disclosure agreements for further protection of our proprietary products and technologies. Protection of our technologies is important for us to offer our customers and partners proprietary services and products that are not available from our competitors, and to exclude our competitors from practicing technology that we have developed or exclusively licensed from other parties. For example, our ability to supply innovator pharmaceutical manufacturers depends on our ability to supply proprietary

enzymes or methods for making pharmaceutical intermediates or APIs that are not available from our competitors. Likewise, in the generic pharmaceutical area, proprietary protection, through patent, trade secret or other protection of our enzymes and methods of producing a pharmaceutical product is important for us and our customers to maintain a lower cost production advantage over competitors.

As of December 31, 2018, we owned or controlled approximately 1,100 issued patents and pending patent applications in the United States and in various foreign jurisdictions. These patents and patent applications include many that are directed to our enabling technologies and specific methods and products that support our business in the pharmaceutical markets. In addition, our portfolio includes applications and patents that support our businesses in the biotherapeutics, molecular diagnostics, food and other markets. Our current intellectual property rights have terms that expire between 2019 and 2039. Our United States intellectual property rights directed to the CodeEvolver® proprietary enabling technology platform developed internally by us have terms that expire between 2029 to 2034. Our current intellectual property rights also include patents, trademarks, copyrights, software and certain assumed contracts that we acquired from Maxygen, Inc. ("Maxygen") in October 2010, which are associated with directed evolution technology, known as the MolecularBreeding™ technology platform developed by Maxygen. The intellectual property rights and assets that we acquired from Maxygen continue to be subject to existing exclusive and non-exclusive license rights granted by Maxygen to third parties. We continue to file new patent applications, for which terms generally extend 20 years from the non-provisional filing date in the United States.

As of December 31, 2018, we owned and used the following registered, pending, and common law trademarks in the United States, with some trademarks also registered or pending in foreign jurisdictions: Codexis®, Codex®, CodeEvolver®, Mosaic®, Sage®, Microcyp®, MCYP®, ProSAR®, Unlock the Power of Proteins®, Codexis Protein Engineering Experts™, and a Codexis design mark (i.e., the Codexis logo).

COMPETITION

We face differing forms of competition in the small molecule pharmaceuticals, biotherapeutics, and fine chemicals markets, as set forth below.

Small Molecule Pharmaceuticals

We market our protein catalyst products and services to manufacturers of small molecule pharmaceutical intermediates and APIs. Our primary competitors in that market are companies marketing either conventional, non-enzymatic catalysts or alternative protein catalyst products and services. We also face competition sometimes from existing in-house technologies (both biocatalysts and conventional catalysts) within our client and potential client companies. The principal methods of competition and competitive differentiation in this market are price, product quality and performance, including manufacturing yield, safety and environmental benefits and speed of delivery of product. Pharmaceutical manufacturers that use biocatalytic processes can face increased competition from manufacturers that use more conventional processes and/or manufacturers that are based in regions (such as India and China) with lower regulatory, safety and environmental costs.

The market for the manufacture and supply of APIs and intermediates is large with many established companies. These companies include many of our large innovator and generic pharmaceutical customers, such as Merck, GSK, Pfizer, Bristol Myers Squibb and Teva Pharmaceutical Industries Ltd., which have significant internal research and development efforts directed at developing processes to manufacture APIs and intermediates. The processes used by these companies include classical conventional organic chemistry reactions, chemo catalytic reactions, biocatalytic reactions or combinations thereof. Our protein catalyst based manufacturing processes must compete with these internally developed routes.

Companies developing and marketing conventional catalysts include Solvias AG, BASF, Johnson-Mathey, and Takasago International Corporation.

The market for supplying enzymes for use in pharmaceutical manufacturing is quite fragmented. There is competition from large industrial enzyme companies, such as Novozymes, as well as subsidiaries of larger contract research/contract manufacturing organizations ("CRO/CMO"), such as Royal DSM N.V. ("DSM"), Cambrex Corporation and Almac Group Ltd. There is also competition in the customized and optimized enzyme area from several smaller companies, such as BRAIN AG, Arzeda, c-LEcta GmbH and Evocatal GmbH.

We believe that our principal advantage is our ability to rapidly deliver customized protein catalysts for existing and new intermediates and APIs in the pharmaceutical manufacturing market. This capability has allowed us to create a

breadth of protein catalysts with improved performance characteristics including, for example, better activity, stability, and activity on a range of substrates, compared to traditional chemistry-based manufacturing processes and naturally occurring (and thus not optimized) biocatalysts. We believe that our CodeEvolver® protein engineering platform technology provides substantially superior results, in shorter time frames, than companies offering competing biocatalyst development services.

Biotherapeutics

There are other companies that participate in the biotherapeutics market generally and the PKU market specifically. Many of these companies are large, successful and well-capitalized. BioMarin Pharmaceutical Inc. ("BioMarin") and Daiichi Sankyo Company market Kuvan® in the United States, Europe and Japan for the treatment of a certain type of PKU. In addition, BioMarin gained US FDA approval in 2018 and began commercial sales of Palynziq™ as an injectable enzyme substitution therapy for the potential treatment of PKU. Synlogic is developing SYNB1618 as a potential treatment for PKU, and in 2018, they completed a phase 1/2a clinical trial using SYNB1618. Takeda (who recently acquired Shire Plc), Genzyme / Sanofi S.A. and other companies market or are actively developing new enzyme therapeutics. There are numerous companies that are developing other forms of therapeutics, such as small molecules and gene therapy, which could compete with biotherapeutics.

Fine Chemicals

We entered the fine chemicals market in 2013 by applying our protein engineering technology in the food market. We face similar forms of competition in this market as in the small molecule pharmaceutical markets, with the exception that the risk of losing opportunities to larger competitors in fine chemicals is greater given the larger scale of opportunities available in the fine chemicals market compared to the pharmaceutical market. Our significant competitors in the fine chemicals markets include companies that have been in these marketplaces for many years, such as DuPont Industrial Biosciences (DuPont Genencor), DSM, Novozymes and A.B. Enzymes. These companies have greater resources in these markets than we do and have long-term supply arrangements already in place with customers. Our ability to compete in these markets may be limited by our relatively late entrance. We also face competition in both the fine chemicals and small molecule pharmaceutical markets from emerging companies, like Zymergen and Gingko Bioworks who offer engineered microbe metabolic pathway approaches to these markets.

Core Technology

We are a leader in the field of protein engineering to create novel biocatalysts. Both our pharmaceuticals and fine chemicals businesses rely on our core technology. We are aware that other companies, organizations and persons have developed technologies that appear to have some similarities to our patented proprietary technologies. For example, we are aware that other companies, including DSM and BASF, have alternative methods for obtaining and generating genetic diversity or use mutagenesis techniques to produce genetic diversity. In addition, academic institutions such as the California Institute of Technology, the Max Planck Institute and the Austrian Centre of Industrial Biotechnology are also working in this field. This field is highly competitive with companies and academic and research institutions actively seeking to develop technologies that could be competitive with our technologies.

Technological developments by others may result in our products and technologies, as well as products manufactured by our customers using our biocatalysts, becoming obsolete. We monitor publications and patents that relate to directed molecular evolution to be aware of developments in the field and evaluate appropriate courses of action in relation to these developments.

Many of our competitors have substantially greater manufacturing, financial, research and development, personnel and marketing resources than we do. As a result, our competitors may be able to develop competing and/or superior technologies and processes, and compete more aggressively and sustain that competition over a longer period of time than we could. Our technologies and products may be rendered obsolete or uneconomical by technological advances or entirely different approaches developed by one or more of our competitors.

OPERATIONS

Our corporate headquarters are located in Redwood City, California and provide general administrative support to our business and are the center of our research, development and business operations. We have limited internal manufacturing capacity at our headquarters in Redwood City. We expect to rely on third-party manufacturers for commercial production of our biocatalysts for the foreseeable future. Our in-house manufacturing is dedicated to producing both Codex® Biocatalyst Panels and Kits and enzymes for use by our customers in pilot scale production. We also supply initial commercial quantities of biocatalysts for use by our collaborators to produce pharmaceutical intermediates and manufacture biocatalysts that we sell. Please see Note 15 in the notes to our Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for a description of our revenues and long-lived assets both within and outside of the United States.

Our research and development operations include efforts directed towards engineering protein catalysts, bioprocess development, cellular engineering, biocatalyst screening, metabolites, strain improvement, fermentation development and process engineering. We conduct enzyme evolution, enzyme production development, microbial bioprocess development, cellular engineering, microbial evolution and process engineering evaluations and design primarily at our headquarters in Redwood City, California. For more information on our research and development expenditures, see Item 8 of this Annual

Report on Form 10-K. Manufacturing of our enzymes is conducted primarily in three locations, at our in-house facility in Redwood City, California and at third-party contract manufacturing organizations, Lactosan, GmbH & Co. KG ("Lactosan") in Kapfenberg, Austria and DPhar SpA ("DPhar") in Agnani, Italy. Generally, we perform smaller scale manufacturing in-house and outsource the larger scale manufacturing and a large percentage of our production of novel enzymes to contract manufacturing organizations.

GOVERNMENT REGULATION

In the United States, the FDA regulates drug and biologic products under the Federal Food, Drug and Cosmetic Act, its implementing regulations and other laws, including, in the case of biologics, the Public Health Service Act. Our biotherapeutic product candidates are subject to regulation by the FDA as biologics. Biologics require the submission of a biologics license application ("BLA") and licensure, which constitutes approval, by the FDA before being marketed in the United States. If we or our development partners fail to comply with applicable FDA or other requirements at any time during product development, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions.

The process required by the FDA before our biologic product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's good laboratory practice ("GLP") regulations;
- submission to the FDA of an IND, which must become effective before clinical trials in the United States may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication, conducted in accordance with the FDA's good clinical practice ("GCP") regulations;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing ("cGMP") regulations; and
- FDA review and approval of the BLA prior to any commercial marketing, sale or distribution of the product.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Preclinical and Clinical Trials

Once a product candidate is identified for development, it enters the preclinical testing stage. Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which must be conducted in accordance with GLP requirements. The results of preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol must be submitted to the FDA as part of the IND. An independent institutional review board ("IRB") for each investigator site proposing to participate in a clinical trial must also review and approve the clinical trial before it can begin at that site, and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP requirements, including requirements for informed consent.

For purposes of BLA approval, clinical trials are typically conducted in three sequential phases, which may overlap or be combined.

- Phase 1-Phase 1 clinical trials involve initial introduction of the investigational product into healthy human subjects or patients with the target disease or condition. These studies are typically designed to test the safety,

dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.

- Phase 2-Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosage and dosing schedule and to identify possible adverse side effects and safety risks.
- Phase 3-Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labeling.

In some cases, the FDA may condition approval of a BLA on the sponsor's agreement to conduct additional clinical trials to further assess the biologic's safety and effectiveness after BLA approval. Such post-approval clinical trials are typically referred to as Phase 4 clinical trials.

Although most clinical research performed in the United States in support of a BLA must be authorized in advance by the FDA, under the IND regulations and procedures described above, there are certain circumstances under which clinical trials can be conducted without submission of an IND. For example, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events, findings from other studies that suggest a significant risk for human subjects, and any clinically important increase in the rate of a serious adverse reaction over that listed in the protocol or investigator brochure.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the biologic and finalize a process for manufacturing the biologic in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and FDA Review

The results of preclinical studies and clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the biologic, are submitted to the FDA in the form of a BLA requesting approval to market the biologic for one or more specified indications. The submission of a BLA requires payment of a substantial user fee unless a waiver is granted. Each BLA submitted to the FDA is reviewed for administrative completeness and reviewability within 60 days of the FDA's receipt of the application. If the BLA is found to be complete, the FDA will file the BLA, triggering a full substantive review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission.

Once a BLA has been accepted for filing, by law the FDA has 180 days to review the application and respond to the applicant. However, the review process is often significantly longer. Under the Prescription Drug User Fee Act, the FDA has a goal of reviewing BLAs within ten months of the 60-day filing date for standard review or six months for priority review, but the overall timeframe is often extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether the biological product is safe, pure and potent and whether the facility or facilities in which it is manufactured meet standards designed to assure the product's continued safety, purity and potency. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving a BLA, the FDA will inspect the facility or the facilities at which the biologic product is manufactured, and will not license the product unless cGMP compliance is satisfactory. The FDA may also inspect the

sites at which the clinical trials were conducted to assess their compliance with GCP requirements.

The FDA may deny approval of a BLA if the applicable statutory and regulatory criteria are not satisfied, or it may require additional preclinical or clinical data. Even if such data are submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than sponsors. Once the FDA approves a BLA, such approval defines the indicated uses for which the biologic may be

marketed. The FDA may also require implementation of a Risk Evaluation and Mitigation Strategy, or REMS, which can include a medication guide, communication plan, or elements to assure safe use, such as restricted distribution methods, physician training, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling claims or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the market. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and it may limit further marketing based on the results of these post-marketing studies. After approval, certain changes to the approved biologic, such as adding new indications, manufacturing changes or additional labeling claims, are subject to further FDA review and approval. Depending on the nature of the proposed change, a BLA supplement must be filed and approved before the change may be implemented.

Post-Approval Requirements

Licensed biologics that are manufactured and distributed in the United States are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product distribution, advertising and promotion and reporting of adverse experiences with the product. There is also a continuing, annual prescription drug program user fee.

Any biologics manufactured or distributed by us, our partners or our contract manufacturers pursuant to FDA approvals would be subject to ongoing regulation by the FDA. Manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose extensive procedural and documentation requirements. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post-market studies or clinical trials to assess new safety risks, imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet and social media. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Physicians may prescribe legally available biologics for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Biosimilars and Regulatory Exclusivity

As part of the Patient Protection and Affordable Care Act enacted in 2010, as amended by the Health Care and Education Reconciliation Act of 2010, the Biologics Price Competition and Innovation Act ("BPCIA") established an

abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory pathway provides legal authority for the FDA to review and approve biosimilar biologics based on their similarity to an existing brand product, referred to as a reference product, including the possible designation of a biosimilar as interchangeable with a brand product. Under the BPCIA, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. Moreover, the extent to which a biosimilar, once approved, will be substituted for a reference product in a way that is similar to traditional generic substitution for non-biological drug products is not yet clear and will depend on a number of marketplace and regulatory factors that are still developing. The BPCIA is complex and continues

to be interpreted and implemented by the FDA. As a result, its ultimate implementation and impact are subject to uncertainty. In addition, the period of exclusivity provided by the BPCIA only operates against third parties seeking approval via the abbreviated pathway, but would not prevent third parties from pursuing approval via the traditional BLA approval pathway.

CUSTOMERS

We rely on a limited number of key customers for the majority of our revenues. Customers that provided 10% or more of our total revenues in any of the past three fiscal years consist of the following:

	Percentage of Total Revenues For The Years Ended December 31,					
	2018		2017		2016	
Customers:						
Merck	29	%	28	%	47	%
Nestlé Health Science	22	%	15	%	*	
Tate & Lyle	13	%	11	%	*	
Novartis	*		14	%	*	
GSK	*		*		22	%

* Percentage was less than 10%

EMPLOYEES

As of December 31, 2018, we had 132 full-time employees and part-time employees worldwide. Of these employees, 77 were engaged in research and development, 18 were engaged in operations and quality control, and 37 were engaged in selling, general and administrative activities. None of our employees is represented by a labor union, and we consider our employee relations to be good.

CORPORATE & AVAILABLE INFORMATION

Our principal corporate offices are located at 200 Penobscot Drive, Redwood City, California 94063 and our telephone number is (650) 421-8100. We were incorporated in Delaware in January 2002. Our internet address is www.codexis.com. The information on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K or any other filings we make with the U.S. Securities and Exchange Commission (the “SEC”).

We make available on or through our website certain reports and amendments to those reports that we file with, or furnish to, the SEC in accordance with the Exchange Act. These include our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC. Copies of this information may be obtained at the SEC website at www.sec.gov. The contents of these websites are not incorporated into this filing. Further, the references to website URLs are intended to be inactive textual references only.

ITEM 1A. RISK FACTORS

You should carefully consider the risks described below together with the other information set forth in this Annual Report on Form 10-K, which could materially affect our business, financial condition or future results. The risks described below are not the only risks facing our company. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition and/or operating results.

Risks Relating to Our Business and Strategy

During our operating history, the markets in which we have participated have changed significantly, which may make it difficult to evaluate our current business and predict our future performance.

Our company has been in existence since January 2002. From 2002 until 2005, our operations focused on organizing and staffing our company and developing our technology platform. In 2005, we recognized our first revenues from product sales. From 2006 to August 2012, a major portion of our business revolved around our research and development collaboration with Shell with respect to advanced biofuels. The Shell collaboration was terminated in August 2012 and did not contribute to our revenues after the termination. As a result of the termination of the Shell collaboration, we undertook a significant restructuring of our operations and refocused our business on the biocatalysis market. In November 2013, we announced that we had begun to wind down our CodeXyme® cellulase enzymes program, and that we had stopped further development of our CodeXol® detergent alcohols program in the third quarter of 2013. Our Novel Biotherapeutics business is relatively new to Codexis. As a result of these changes in our business and any changes to our business focus that we may make as we move forward, our operating history in past periods may not provide a basis to evaluate our current business or be indicative of our future performance. We have encountered and will continue to encounter risks and difficulties frequently experienced by young companies in rapidly changing industries. If we do not address these risks successfully, our business will be harmed.

Our quarterly or annual operating results may fluctuate in the future. As a result, we may fail to meet or exceed the expectations of research analysts or investors, which could cause our stock price to decline.

Our financial condition and operating results have varied significantly in the past and may continue to fluctuate from quarter to quarter and year to year in the future due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include the following factors, as well as other factors described elsewhere in this report:

- our ability to achieve or maintain profitability;
- our relationships with, and dependence on, collaborators in our principal markets;
- our dependence on a limited number of customers;
- our dependence on a limited number of products in our biocatalysis business;
- our reliance on a limited number of contract manufacturers for large scale production of substantially all of our enzyme products;
- our ability to develop and successfully commercialize new products for the biocatalysis market(s);
- our ability to obtain additional development partners for our biotherapeutic programs;
- potential of Nestlé Health Science terminating any development program under its license agreement with us;
- our ability to deploy our technology platform in the fine chemicals market;
- the success of our customers' pharmaceutical products in the market and the ability of such customers to obtain regulatory approvals for products and processes;
- our or our customers' ability to obtain regulatory approval for the sale and manufacturing of food products using our enzymes;
- our ability to deploy our technology platform in the in vitro molecular diagnostics market;
- our ability to successfully achieve domestic and foreign regulatory approval for product candidates;
- our ability to successfully design and execute clinical testing at a reasonable cost and on an acceptable time-frame;
- our dependence on product candidates which could unexpectedly fail at any stage of preclinical or clinical development;

- our dependence on product candidates which may lack the ability to work as intended or cause undesirable side effects;
- our dependency on third parties to conduct clinical trials, research, and preclinical studies;

- our ability to successfully prosecute and protect our intellectual property;
- our ability to compete if we do not adequately protect our proprietary technologies or if we lose some of our intellectual property rights;
- our ability to avoid infringing the intellectual property rights of third parties;
- our involvement in lawsuits to protect or enforce our patents or other intellectual property rights;
- our ability to enforce our intellectual property rights throughout the world;
- our dependence on, and the need to attract and retain, key management and other personnel;
- our ability to prevent the theft or misappropriation of our biocatalysts, the genes that code for our biocatalysts, know-how or technologies;
- our ability to protect our trade secrets and other proprietary information from disclosure by employees and others;
- our ability to obtain substantial additional capital that may be necessary to expand our business;
- our ability to comply with the terms of our credit facility;
- our ability to timely pay debt service obligations;
- our customers' ability to pay amounts owed to us in a timely manner;
- our ability to avoid charges to earnings as a result of any impairment of goodwill, intangible assets or other long-lived assets;
- changes in financial accounting standards or practices may cause adverse, unexpected financial reporting fluctuations and affect our reported results of operations;
- our ability to maintain effective internal control over financial reporting;
- our dependency on information technology systems, infrastructure and data;
- our ability to control and to improve product gross margins;
- our ability to protect against risks associated with the international aspects of our business;
- the cost of compliance with European Union chemical regulations;
- potential advantages that our competitors and potential competitors may have in securing funding or developing products;
- our ability to accurately report our financial results in a timely manner;
- results of regulatory tax examinations;
- business interruptions, such as earthquakes and other natural disasters;
- public concerns about the ethical, legal and social ramifications of genetically engineered products and processes;
- our ability to integrate our current business with any businesses that we may acquire in the future;
- our ability to properly handle and dispose of hazardous materials in our business;
- potential product liability claims;
- uncertainties in the interpretation and application of the 2017 Tax Cuts and Jobs Act and related regulations could materially affect our tax obligations and effective tax rate; and
- our ability to use our net operating loss carryforwards to offset future taxable income.

Due to the various factors mentioned above, and others, the results of any prior quarterly or annual periods should not be relied upon as indications of our future operating performance.

We have a history of net losses and we may not achieve or maintain profitability.

We have incurred net losses since our inception, including losses of $10.9 million in 2018, $23.0 million in 2017 and $8.6 million in 2016. As of December 31, 2018 and 2017, we had an accumulated deficit of $330.5 million and $315.1 million, respectively. If we are unable to expand our biocatalysis business, through new or expanded collaborations, development of new products or services, or increased sales of existing products and services, our net losses may increase and we may never achieve profitability. In addition, some of our collaboration agreements, including our collaboration with Nestlé Health Science, provide for milestone payments and/or future royalty payments, which we will only receive if we and our collaborators develop and commercialize products. We also may fund development of additional proprietary biocatalysis and/or biotherapeutic products. There can be no assurance that any of these products will become commercially viable or that we will ever achieve profitability on a quarterly or annual basis. If we fail to achieve profitability, or if the time required to achieve profitability is longer than we

anticipate, we may not be able to continue our business. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We are dependent on our collaborators, and our failure to successfully manage these relationships could prevent us from developing and commercializing many of our products and achieving or sustaining profitability, and could lead to disagreements with our current or former collaborators.

Our ability to maintain and manage collaborations in our markets is fundamental to the success of our business. We currently have license agreements, research and development agreements, supply agreements and/or distribution agreements with various collaborators. For example, we have ongoing collaborations with GSK, Merck and Nestlé Health Science that are important to our business and financial results. We may have limited or no control over the amount or timing of resources that any collaborator is able or willing to devote to our partnered products or collaborative efforts. Any of our collaborators may fail to perform its obligations. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct their collaborative activities successfully and in a timely manner. Further, our collaborators may not develop products arising out of our collaborative arrangements or devote sufficient resources to the development, manufacture, marketing or sale of these products. Moreover, disagreements with a collaborator could develop, and any conflict with a collaborator could lead to litigation and could reduce our ability to enter into future collaboration agreements and negatively impact our relationships with one or more existing collaborators. If any of these events occur, especially if they occur in our collaborations with GSK, Merck or Nestlé Health Science, or if we fail to maintain our agreements with our collaborators, we may not be able to commercialize our existing and potential products or grow our business or generate sufficient revenues to support our operations, we may not receive contemplated milestone payments and royalties under the collaboration, and we may be involved in litigation. Our collaboration opportunities could be harmed and our financial condition and results of operations could be negatively affected if:

- we do not achieve our research and development objectives under our collaboration agreements in a timely manner or at all;
- we develop products and processes or enter into additional collaborations that conflict with the business objectives of our other collaborators;
- we, our collaborators and/or our contract manufacturers do not receive the required regulatory and other approvals necessary for the commercialization of the applicable product;
- we disagree with our collaborators as to rights to intellectual property that are developed during the collaboration, or their research programs or commercialization activities;
- we are unable to manage multiple simultaneous collaborations;
- our collaborators or licensees are unable or unwilling to implement or use the technology or products that we provide or license to them;
- our collaborators become competitors of ours or enter into agreements with our competitors;
- our collaborators become unable or less willing to expend their resources on research and development or commercialization efforts due to general market conditions, their financial condition or other circumstances beyond our control; or
- our collaborators experience business difficulties, which could eliminate or impair their ability to effectively perform under our agreements.

Even after collaboration relationships expire or terminate, some elements of the collaboration may survive. For instance, certain rights, licenses and obligations of each party with respect to intellectual property and program materials may survive the expiration or termination of the collaboration. Disagreements or conflicts between and among the parties could develop even though the collaboration has ended. These disagreements or conflicts could result in expensive arbitration or litigation, which may not be resolved in our favor.

Finally, our business could be negatively affected if any of our collaborators or suppliers undergoes a change of control or were to otherwise assign the rights or obligations under any of our agreements.

We are dependent on a limited number of customers.

Our current revenues are derived from a limited number of key customers. For the year ended December 31, 2018 and 2017, customers that each individually contributed 10% or more of our total revenue accounted for 64% and 68% of our total revenues in 2018 and 2017, respectively. We expect a limited number of customers to continue to account for a significant portion of our revenues for the foreseeable future. This customer concentration increases the risk of

quarterly fluctuations in our revenues and operating results. The loss or reduction of business from one or a combination of our significant customers could, materially adversely affect our revenues, financial condition and results of operations.

We are dependent on a limited number of products in our protein catalysts business.

Our current product sales are derived from a limited number of protein catalyst products. We expect a limited number of protein catalyst products to continue to account for a significant portion of our product sales for the foreseeable future. This product concentration increases the risk of quarterly fluctuations in our revenues and operating results. The loss or reduction of business of one or a combination of our significant products could materially adversely affect our revenues, financial condition and results of operations.

We are dependent on a limited number of contract manufacturers for large scale production of substantially all of our enzymes.

Manufacturing of our enzymes is conducted primarily in three locations: our in-house facility in Redwood City, California, and at two third-party contract manufacturing organizations, Lactosan, GmbH & Co. KG ("Lactosan"), in Kapfenberg, Austria, and DPhar SpA (“DPhar”), in Agnani, Italy. Generally, we perform smaller scale manufacturing in-house and outsource the larger scale manufacturing to these contract manufacturers. We have limited internal capacity to manufacture enzymes. As a result, we are dependent upon the performance and capacity of third-party manufacturers for the larger scale manufacturing of the enzymes used in our pharmaceutical and fine chemicals business.

Accordingly, we face risks of difficulties with, and interruptions in, performance by third party manufacturers, the occurrence of which could adversely impact the availability, launch and/or sales of our enzymes in the future. Manufacturing delays at a contract manufacturer could negatively affect our business, reputation, results of operations and financial condition. The failure of any contract manufacturer to supply us enzymes on a timely basis, or to manufacture our enzymes in compliance with our specifications or applicable quality requirements or in volumes sufficient to meet demand, would adversely affect our ability to sell pharmaceutical and fine and complex chemicals products, could harm our relationships with our collaborators or customers and could negatively affect our revenues and operating results. We may be forced to secure alternative sources of supply, which may be unavailable on commercially acceptable terms, and could cause delays in our ability to deliver products to our customers, increase our costs and decrease our profit margins.

We currently have supply agreements in place with Lactosan and DPhar. In the absence of a supply agreement, a contract manufacturer will be under no obligation to manufacture our enzymes and could elect to discontinue their manufacture at any time. If we require additional manufacturing capacity and are unable to obtain it in sufficient quantity, we may not be able to increase our product sales, or we may be required to make substantial capital investments to build that capacity or to contract with other manufacturers on terms that may be less favorable than the terms we currently have with our suppliers. If we choose to build our own additional manufacturing facility, it could take two years or longer before our facility is able to produce commercial volumes of our enzymes. Any resources we expend on acquiring or building internal manufacturing capabilities could be at the expense of other potentially more profitable opportunities. In addition, if we contract with other manufacturers, we may experience delays of several months in qualifying them, which could harm our relationships with our collaborators or customers and could negatively affect our revenues or operating results.

If we are unable to develop and commercialize new products for the pharmaceutical, fine chemicals, biotherapeutics and molecular diagnostics markets, our business and prospects will be harmed.

We plan to launch new products for the pharmaceutical, fine chemicals, therapeutics and molecular diagnostics markets. These efforts are subject to numerous risks, including the following:

- customers in these markets may be reluctant to adopt new manufacturing processes that use our enzymes;
- we may be unable to successfully develop the enzymes or manufacturing processes for our products in a timely and cost-effective manner, if at all;
- we may face difficulties in transferring the developed technologies to our customers and the contract manufacturers that we may use for commercial scale production of intermediates and enzymes in these markets;
- the contract manufacturers that we may use may be unable to scale their manufacturing operations to meet the demand for these products and we may be unable to secure additional manufacturing capacity;
- customers may not be willing to purchase these products for these markets from us on favorable terms, if at all;
- we may face product liability litigation, unexpected safety or efficacy concerns and product recalls or withdrawals;
-

changes in laws or regulations relating to the pharmaceutical industry or the industries into which we sell our fine chemicals products, including the food industry, could cause us to incur increased costs of compliance or otherwise harm our business;

- our customers' products may experience adverse events or face competition from new products, which would reduce demand for our products;

- we may face pressure from existing or new competitive products; and
- we may face pricing pressures from existing or new competitors, some of which may benefit from government subsidies or other incentives.

Our biotherapeutic programs are early stage, highly regulated and expensive. Our ability to obtain additional development partners for the programs, to advance our product candidates to clinical trials and to ultimately receive regulatory approvals is highly uncertain.

We are developing and have developed novel biotherapeutic candidates, including CDX-6114, our novel oral enzyme product candidate for the treatment of PKU. The successful development of biotherapeutic candidates involves many risks and uncertainties, requires long timelines and may lead to uncertain results. In addition, drug development is highly regulated and requires areas of expertise and capital resources we do not currently possess. In order to market a drug product in the United States, we must undergo the following process required by the FDA:

- completion of extensive preclinical laboratory tests and preclinical animal studies, all performed in accordance with GLP requirements;
- submission to the FDA of an IND, which must become effective before human clinical studies may begin in the United States;
- approval by an independent IRB representing each clinical site before the clinical study may be initiated at the site;
- performance of adequate and well-controlled human clinical studies (generally divided into three phases) in accordance with GCP requirements to establish the safety and efficacy of the product candidate for each proposed indication;
- preparation of and submission to the FDA of a BLA after completion of all clinical studies;
- potential review of the product candidate by an FDA advisory committee;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the product candidate is produced to assess compliance with cGMP requirements; and
- FDA review and approval of a BLA prior to any commercial marketing or sale of the product in the United States.

If we fail to comply with applicable FDA or other regulatory requirements at any time during the drug development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial penalties, including the FDA's refusal to approve a pending application, withdrawal of an approval, warning letters, product recalls, and additional enforcement actions.

In October 2017, we entered into a Global Development, Option and License Agreement with Nestlé Health Science ("Nestlé Agreement") pursuant to which we granted to Nestlé Health Science an option to obtain an exclusive, worldwide, royalty-bearing, sublicenseable license to develop and commercialize certain products based on our therapeutic enzyme product candidates for the treatment of hyperphenylalaninemia ("HPA"), including CDX-6114, as well as an exclusive right of first negotiation to obtain an exclusive worldwide license to develop and commercialize any enzyme discovered by us for use in the field of the prevention, diagnosis, treatment and management of inborn errors of amino acid metabolism. HPA is a medical condition characterized by mildly or strongly elevated concentrations of the amino acid phenylalanine in the blood. PKU can result in severe HPA. In February 2019, Nestlé Health Science exercised its option to receive an exclusive license to further develop and commercialize CDX-6114 and our other therapeutic enzyme product candidates covered by specified patent applications for the treatment of PKU.

Our efforts to advance our biotherapeutic candidates that we develop are subject to numerous risks, including the following:

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and the results are inherently unpredictable. If we are ultimately unable to obtain regulatory approval for biotherapeutic product candidates, our business will be harmed. To obtain regulatory approval to market any product candidate,

- preclinical studies and costly and lengthy clinical trials are required, and the results of the studies and trials are highly uncertain. A failure of one or more pre-clinical or clinical trials can occur at any stage, and many companies that have believed their drug candidates performed satisfactorily in pre-clinical and clinical testing have nonetheless failed to obtain marketing approval of their product candidates.
-

We may find it difficult to enroll patients in our clinical trials for product candidates. Any enrollment difficulties could delay clinical trials and any potential product approval.

- We may experience difficulty or delay in obtaining the FDA's acceptance of an IND for product candidates we may seek to enter into clinical development, which would delay initiation of Phase 1 clinical testing. Delays in the

commencement or completion of clinical testing could significantly affect our product development costs or the product development costs of our present and any future collaborators. We do not know whether planned clinical trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons. For example, a clinical trial may be suspended or terminated by us, by the IRB of the institution in which such trial is being conducted, or by the FDA due to a number of factors, including unforeseen safety issues, changes in governmental regulations or lack of adequate funding to continue the clinical trial.

- We have limited experience in drug development or regulatory matters related to drug development. As a result, we rely or will rely on third parties to conduct our pre-clinical and clinical studies, assist us with drug manufacturing and formulation and perform other tasks for us. If these third parties do not successfully carry out their responsibilities or comply with regulatory requirements, we may receive lower quality products or services, suffer reputational harm and not be able to obtain regulatory approval for product candidates.
- Our efforts to use CodeEvolver® protein engineering technology platform to generate new lead biotherapeutic candidates, whether under our collaboration with Nestlé Health Science or otherwise, may not be successful in creating candidates of value.
- We will be exposed to potential product liability risks through the testing of experimental therapeutics in humans, which may expose us to substantial uninsured liabilities.
- Third parties may develop intellectual property that could limit our ability to develop, market and commercialize product candidates.
- Changes in methods of treatment of disease, such as gene therapy, could cause us to stop development of our product candidate or reduce or eliminate potential demand for CDX-6114, if approved, or any other product candidates that we may develop in the future.

If Nestlé Health Science terminates its development program under its license agreement with us, any potential revenue from that license agreement will be significantly reduced or non-existent, and our results of operations and financial condition will be materially and adversely affected.

We have invested significant time and financial resources in the development of CDX-6114 and other product candidates for the treatment of HPA now included in the Nestlé Agreement (each a “Compound”).

In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, Nestlé Health Science is obligated to pay us $3.0 million within 60 days after exercise of the option. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, “Subsequent Events” in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details.

Under the Nestlé Agreement, we are eligible to receive from Nestlé Health Science development and approval milestones of up to $86.0 million, sales-based milestones of up to $250.0 million, and tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of products containing a licensed Compound as its sole active ingredient. We have received milestone payments under the Nestlé Agreement to date. However, there is no guarantee that we will receive further milestone payments under the Nestlé Agreement.

Nestlé Health Science may terminate the entire agreement in the event of serious safety issues related to any Compound or product subject to the agreement and at its convenience. We may terminate the Nestlé Agreement if Nestlé Health Science challenges the validity or enforceability of any of our patents covering the Compound. Either party may terminate the agreement in the event of the other party’s uncured material breach or insolvency. Depending on the timing of any such termination, we may not be entitled to receive potential milestone payments, as these payments terminate with termination of the Nestlé Agreement.

If Nestlé Health Science terminates its rights and obligations with respect to the Nestlé Agreement, then depending on the timing of such event:

- the development of our product candidates subject to the agreement may be terminated or significantly delayed;

- our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate scarce resources to the development and commercialization of product candidates;

- we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of the Nestlé Agreement, including the reimbursement of third parties; and in order to fund further development and commercialization of new product candidates or programs, we may need to seek out and establish alternative collaboration arrangements with third-party partners; this may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of one or more of our programs or increase our expenditures and seek additional funding by other means.

Our efforts to deploy our technology platform in the fine chemicals market may fail.

We have recently begun to use our CodeEvolver® protein engineering technology platform to develop new products in the fine chemicals markets. We do not know if we can successfully compete in this new market. This new market is well established and consists of numerous large, well-funded entrenched market participants who have long and established track records and customer relationships. We have currently developed products in the food sector of this market and these products, or any other products that we may develop in the future for the fine chemicals market may not succeed in displacing current products. If we succeed in commercializing new products for the fine chemicals market, we may not generate significant revenues and cash flows from these activities. The failure to successfully deploy products in the fine chemicals space may limit our growth and have a material adverse effect on our financial condition, operating results and business prospects.

Our business could be adversely affected if our customers' products are not received well in the market, if their products, or the processes used by our customers to manufacture their final products, fail to be approved, or if our customers discontinue their development activities for any reason.

Our enzymes are used by our pharmaceutical customers in the manufacture of intermediates and APIs which are then used in the manufacture of final pharmaceutical products by our existing and potential branded and generic drug customers, and by our fine chemicals customers to manufacture food ingredients. Our business could be adversely affected if these final products do not perform in the market as well as expected, or if our customers encounter competition from new entrants into the market with competing, and possibly superior, products. Additionally, many of these pharmaceutical and food products must be reviewed and approved by the FDA in the United States and similar regulatory bodies in other markets prior to commercialization. If our customers who sell branded drugs, which we refer to as innovators, fail to receive regulatory approval for the drugs, fail to receive regulatory approval for new manufacturing processes for previously approved drugs, or decide for business or other reasons to discontinue their drug development activities, our revenues and prospects will be negatively impacted. The process of producing these drugs, and their generic equivalents, is also subject to regulation by the FDA in the United States and equivalent regulatory bodies in other markets. Similarly, if our food ingredient product and other fine chemical customers were to delay or discontinue development on their products, our revenues and prospects will be negatively impacted. If any pharmaceutical or food manufacturing process that uses our enzymes or enzyme technology does not receive required approval by the appropriate regulatory body or if customers decide not to pursue approval, our business could be adversely affected.

We or our customers may not be able to obtain regulatory approval for the use of our products in food and food ingredients, if required, and, even if approvals are obtained, complying on an ongoing basis with the numerous regulatory requirements applicable to these products will be time-consuming and costly.

The products that we develop for our food and food ingredient customers are, and any other products that we may develop for the food and food ingredients market will likely be, subject to regulation by various government agencies, including the FDA, state and local agencies and similar agencies outside the United States, as well as religious compliance certifying organizations. Food ingredients are regulated by the FDA either as food additives or as substances generally recognized as safe ("GRAS"). A substance can be listed or affirmed as GRAS by the FDA or self-affirmed by its manufacturer upon determination that independent qualified experts would generally agree that the substance is GRAS for a particular use. While we generally self-affirm GRAS status for the products that we develop for the food market, our customer(s) will need to submit a GRAS Notice of Determination for its final commercial product. There can be no assurance that our customer(s) will not receive any objections from the FDA to their Notice of Determination. If the FDA were to disagree with our customer's determination, they could ask our customer to voluntarily withdraw the final commercial product from the market or could initiate legal action to halt its sale. Such

actions by the FDA could have an adverse effect on our business, financial condition, and results of our operations. Food ingredients that are not GRAS are regulated as food additives and require FDA approval prior to commercialization. The food additive petition process is generally expensive and time consuming, with approval, if secured, potentially taking years.

Changes in regulatory requirements, laws and policies, or evolving interpretations of existing regulatory requirements, laws and policies, may result in increased compliance costs, delays, capital expenditures and other financial obligations that could adversely affect our business or financial results.

We expect to encounter regulations in most if not all of the countries in which we may seek to sell our products which are used in food and food ingredients, and we cannot be sure that we or our customers will be able to obtain necessary approvals in a timely manner or at all. If our existing and future products which are used in food and food ingredients do not meet applicable regulatory requirements in a particular country or at all, then we may not be able to commercialize them and our business will be adversely affected. The various regulatory schemes applicable to our products which are used in food and food ingredients will continue to apply following initial approval for sale, including FDA requirements for food safety, mandatory labeling, and certain nutrient content or health claims made about the product. Monitoring regulatory changes and ensuring our ongoing compliance with applicable requirements will be time-consuming and may affect our results of operations. If we fail to comply with such requirements on an ongoing basis, we may be subject to fines or other penalties, or may be prevented from selling our products which are used in food and food ingredients and our business may be harmed.

Our efforts to deploy our technology in the in vitro molecular diagnostics market may fail.

We have recently begun to use our CodeEvolver® protein engineering technology platform to develop new products for customers using NGS and PCR/qPCR for in vitro molecular diagnostic applications. We do not know if we can successfully compete in this new market. This new market is well established and consists of numerous large, well-funded entrenched market participants who have long and established track records and customer relationships. Our first proprietary enzyme for this market, which is designed to improve library preparation for NGS users, and any products that we may develop in the future for this market, may not succeed in displacing current products. If we succeed in commercializing new products for this market, we may not generate significant revenues and cash flows from these activities. The failure to successfully deploy products on timely basis in this space may limit our growth and have a material adverse effect on our financial condition, operating results and business prospects.

Interim “top-line” and preliminary data from studies or trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim “top-line” or preliminary data from preclinical studies or clinical trials. Interim data are subject to the risk that one or more of the outcomes may materially change as more data become available. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary or “top-line” data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Additionally, interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could significantly harm our

business prospects.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

We and any collaborators are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. To date, neither we nor our collaborators have submitted a BLA to FDA or similar drug approval submissions to comparable foreign regulatory authorities for any product candidate. We and any collaborators must complete additional preclinical or nonclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the regulatory authorities before we will be able to obtain these approvals. Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our or our collaborators' clinical trials;
- we or our collaborators may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we or our collaborators may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our or our collaborators' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of product candidates may not be sufficient to support the submission of a BLA to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may fail to approve the companion diagnostics we contemplate developing with collaborators; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a REMS. Regulatory authorities may not approve the price we or our collaborators intend to charge for products we may develop, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Clinical trials are difficult to design and implement, expensive, time-consuming and involve an uncertain outcome, and the inability to successfully conduct clinical trials and obtain regulatory approval for our product candidates would substantially harm our business.

Clinical testing is expensive and usually takes many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, and product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. We do not know whether planned clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Clinical trials can be delayed, suspended or terminated for a variety of reasons, including in connection with:

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the inability to generate sufficient preclinical, toxicology or other in vivo or in vitro data to support the initiation of clinical trials;

- applicable regulatory authorities disagreeing as to the design or implementation of the clinical trials;
- obtaining regulatory authorization to commence a trial;

- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining IRB approval at each site;
- developing and validating the companion diagnostic to be used in a clinical trial, if applicable;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- recruiting and retaining enough suitable patients to participate in a trial;
- having enough patients complete a trial or return for post-treatment follow-up;
- adding a sufficient number of clinical trial sites;
- inspections of clinical trial sites or operations by applicable regulatory authorities, or the imposition of a clinical hold;
- clinical sites deviating from trial protocol or dropping out of a trial;
- the inability to demonstrate the efficacy and benefits of a product candidate;
- discovering that product candidates have unforeseen safety issues, undesirable side effects or other unexpected characteristics;
- addressing patient safety concerns that arise during the course of a trial; receiving untimely or unfavorable feedback from applicable regulatory authorities regarding the trial or requests from regulatory authorities to modify the design of a trial;
- non-compliance with applicable regulatory requirements by us or third parties or changes in such regulations or administrative actions;
- suspensions or terminations by IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities due to a number of factors, including those described above;
- third parties being unable or unwilling to satisfy their contractual obligations to us; or
- changes in our financial priorities, greater than anticipated costs of completing a trial or our inability to continue funding the trial.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Additionally, we or our collaborators may experience unforeseen events during or resulting from clinical trials that could delay or prevent receipt of marketing approval for or commercialization of product candidates. For example, clinical trials of product candidates may produce negative, inconsistent or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs. Regulators may also revise the requirements for approving the product candidates, or such requirements may not be as we anticipate. If we or our collaborators are required to conduct additional clinical trials or other testing of product candidates beyond those that we or our collaborators currently contemplate, if we or our collaborators are unable to successfully complete clinical trials or other testing of such product candidates, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining or fail to obtain marketing approval for product candidates;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements;
- be subject to changes in the way the product is administered;
- have regulatory authorities withdraw or suspend their approval of the product or impose restrictions on its distribution;
- be sued; or

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- experience damage to our reputation.

If we or our collaborators experience delays in the commencement or completion of our clinical trials, or if we or our collaborators terminate a clinical trial prior to completion, we may experience increased costs, have difficulty raising capital and/or be required to slow down the development and approval process timelines. Furthermore, the product candidates that are the subject of such trials may never receive regulatory approval, and their commercial prospects and our ability to generate product revenues from them could be impaired or not realized at all.

We or our collaborators may experience delays or difficulties in enrolling patients in clinical trials, which could delay or prevent receipt of regulatory approvals.

We or our collaborators may not be able to initiate or continue clinical trials on a timely basis or at all for any product candidates we or our collaborators identify or develop if we or our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. Additionally, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as one or more of our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in our competitors' clinical trials. Patient enrollment may also affected by many factors, including:

- severity and difficulty of diagnosing of the disease under investigation;
- size of the patient population and process for identifying subjects;
- eligibility and exclusion criteria for the trial in question;
- our or our collaborators' ability to recruit clinical trial investigators with the appropriate competencies and experience;
- design of the trial protocol;
- availability and efficacy of approved medications or therapies, or other clinical trials, for the disease or condition under investigation;
- perceived risks and benefits of the product candidate under trial or testing, or of the application of genome editing to human indications;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

We expect that some of our product candidates will focus on diseases with limited patient pools from which to draw for enrollment in clinical trials. The eligibility criteria of our clinical trials will further limit the pool of available trial participants. In addition to the factors identified above, patient enrollment in any clinical trials we or our collaborators may conduct may be adversely impacted by any negative outcomes our competitors may experience, including adverse side effects, clinical data showing inadequate efficacy or failures to obtain regulatory approval. Enrollment delays in clinical trials may result in increased development costs for any of our product candidates, which may cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which may have an adverse effect on our results of operations and prospects.

Results of preclinical studies and early clinical trials of product candidates may not be predictive of results of later studies or trials. Our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval.

Preclinical and clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the preclinical study or clinical trial process. Despite promising preclinical or clinical results, any product candidate can unexpectedly fail at any stage of preclinical or clinical development. The historical failure rate for product candidates in our industry is high. The results from preclinical studies or early clinical trials of a product candidate may not be predictive of the results from later preclinical studies or clinical trials, and interim results of a clinical

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trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials.

Many companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks at later stages of development after achieving positive results in early stages of development, and we may face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including previously unreported adverse events. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain regulatory approval. Even if any product candidates progress to clinical trials, these product candidates may fail to show the safety and efficacy in clinical development required to obtain regulatory approval, despite the observation of positive results in animal studies. Our or our collaborators' failure to replicate positive results from early research programs and preclinical or greenhouse studies may prevent us from further developing and commercializing those or other product candidates, which would limit our potential to generate revenues from them and harm our business and prospects.

For the foregoing reasons, we cannot be certain that any ongoing or future preclinical studies or clinical trials will be successful. Any safety or efficacy concerns observed in any one of our preclinical studies or clinical trials in a targeted area could limit the prospects for regulatory approval of product candidates in that and other areas, which could have a material adverse effect on our business and prospects.

If any of our product candidates do not work as intended or cause undesirable side effects, it could hinder or prevent receipt of regulatory approval or realization of commercial potential for them or our other product candidates and could substantially harm our business.

Our product candidates may be associated with serious adverse events, undesirable side effects or unexpected characteristics. Results of clinical trials could reveal severe or recurring side effects, toxicities or unexpected events. In addition to serious adverse events or side effects caused by product candidates we develop alone or with collaborators, the administration process or related procedures may also cause undesirable side effects. If any such events occur, clinical trials or commercial distribution of any product candidates or products we develop alone or with collaborators could be suspended or terminated, and our business and reputation could suffer substantial harm. Treatment-related side effects could affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us or our collaborators to cease further development of, deny approval of or require us to cease selling any product candidates or products for any or all targeted indications. If we or our collaborators elect, or are required, to delay, suspend or terminate any clinical trial or commercialization efforts, the commercial prospects of such product candidates or products may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated.

Additionally, if we successfully develop a product candidate alone or with collaborators and it receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We or our collaborators may also be required to adopt a REMS or engage in similar actions, such as patient education, certification of health care professionals or specific monitoring, if we or others later identify undesirable side effects caused by any product that we develop alone or with collaborators. Such identification could also have several additional significant negative consequences, such as:

- regulatory authorities may suspend, withdraw or limit approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including "boxed" warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;

- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product is administered or conduct additional trials;
- the product may become less competitive;
- we or our collaborators may decide to remove the product from the marketplace;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;

- we could be sued and be held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us or our collaborators from achieving or maintaining market acceptance of any potential product.

Even if we obtain regulatory approval for any products that we develop alone or with collaborators, such products will remain subject to ongoing regulatory requirements, which may result in significant additional expense.

Even if products we develop alone or with collaborators receive regulatory approval, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, among other things. Any regulatory approvals received for such products may also be subject to limitations on the approved indicated uses for which they may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing and surveillance studies. For example, the holder of an approved BLA in the United States is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. In the United States, the holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Similar provisions apply in the EU. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. Similarly, in the EU any promotion of medicinal products is highly regulated and, depending on the specific jurisdiction involved, may require prior vetting by the competent national regulatory authority. In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application.

If we, our collaborators or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory agency may impose restrictions relative to that product, the manufacturing facility or us or our collaborators, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

Moreover, if any of our product candidates are approved, our product labeling, advertising, promotion and distribution will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we or our collaborators fail to comply with applicable regulatory requirements following approval of any potential products we may develop, authorities may:

- issue an untitled enforcement letter or a warning letter asserting a violation of the law;
- seek an injunction, impose civil and criminal penalties, and impose monetary fines, restitution or disgorgement of profits or revenues;
- suspend or withdraw regulatory approval;
- suspend or terminate any ongoing clinical trials or implement requirements to conduct post-marketing studies or clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our collaborators;
- restrict the labeling, marketing, distribution, use or manufacturing of products;
- seize or detain products or otherwise require the withdrawal or recall of products from the market;
- refuse to approve pending applications or supplements to approved applications that we or our collaborators submit;
- refuse to permit the import or export of products; or
- refuse to allow us or our collaborators to enter into government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our or our collaborators' ability to commercialize products and our ability to generate revenues.

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In addition, the FDA's policies, and policies of foreign regulatory agencies, may change, and additional regulations may be enacted that could prevent, limit or delay regulatory approval of product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of biologics and spur innovation. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements, or if we or our collaborators are unable to maintain regulatory compliance, marketing approval that has been obtained may be lost.

Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Our product candidates for which we intend to seek approval as a biologic products may face competition sooner than anticipated.

The BCPIA enacted in the Patient Protection and Affordable Care Act, signed into law on March 23, 2010, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when the FDA will fully adopt processes intended to implement BPCIA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in

a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

We rely on third parties to conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development

programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are and expect to remain dependent on third parties to conduct clinical trials of our product candidates. Specifically, we expect CROs, clinical investigators, and consultants to play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to stop and/or repeat clinical trials, which would delay the marketing approval process.

There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise performs in a substandard manner, or terminates its engagement with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, clinical trial investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable foreign regulatory authorities concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit by the FDA or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our product candidates.

We contract with third parties for the manufacturing and supply of product candidates for use in preclinical testing and clinical trials and related services, which supply may become limited or interrupted or may not be of satisfactory quality and quantity.

We do not have any manufacturing facilities. We produce in our laboratory relatively small quantities of products for evaluation in our research programs. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates are approved. We currently have limited manufacturing arrangements and expect that each of our product candidates will only be covered by single source suppliers for the foreseeable future. This reliance increases the risk that we will not have sufficient quantities of our product candidates or products, if approved, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Furthermore, all entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured in accordance with cGMP requirements. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants, or to inadvertent changes in the properties or stability of our product candidates that

may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's cGMP regulations enforced by the FDA through its facilities inspection program. Comparable foreign regulatory authorities may require compliance with similar requirements. The facilities and quality systems of our third-party contractor manufacturers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of marketing approval of our product candidates. We do not control the manufacturing activities of, and are completely dependent on, our contract manufacturers for compliance with cGMP regulations.

In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on commercially reasonable terms, if at all. In particular, any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. In addition, certain of our product candidates and our own proprietary methods have never been produced or implemented outside of our company, and we may therefore experience delays to our development programs if and when we attempt to establish new third party manufacturing arrangements for these product candidates or methods. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

Our or a third party's failure to execute on our manufacturing requirements, do so on commercially reasonable terms and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of our product candidates under development;
- delay in submitting regulatory applications, or receiving marketing approvals, for our product candidates;
- loss of the cooperation of future collaborators;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease development or to recall batches of our product candidates; and
- in the event of approval to market and commercialize our product candidates, an inability to meet commercial demands for our product or any other future product candidates.

Our efforts to prosecute and protect our intellectual property may not be successful.

We will continue to file and prosecute patent applications and maintain trade secrets in an ongoing effort to protect our intellectual property. It is possible that our current patents, or patents which we may later acquire, may be successfully challenged or invalidated in whole or in part. It is also possible that we may not obtain issued patents from our pending patent applications or other inventions we seek to protect. We sometimes permit certain intellectual property to lapse or go abandoned under appropriate circumstances. Due to uncertainties inherent in prosecuting patent applications, sometimes patent applications are rejected and we subsequently abandon them. It is also possible that we may develop proprietary products or technologies in the future that are not patentable or that the patents of others will limit or altogether preclude our ability to conduct business. In addition, any patent issued to us may provide us with little or no competitive advantage, in which case we may abandon such patent or license it to another entity.

Our means of protecting our proprietary rights may not be adequate and our competitors may independently develop technology or products that are similar to ours or that compete with ours. Patent, trademark, and trade secret laws afford only limited protection for our technology platform and products. The laws of many countries do not protect our proprietary rights to as great an extent as do the laws of the United States. Despite our efforts to protect our proprietary rights, unauthorized parties have in the past attempted, and may in the future attempt, to operate under aspects of our intellectual property or products or to obtain and use information that we regard as proprietary. Third parties may also design around our proprietary rights, which may render our protected technology and products less valuable, if the design around is favorably received in the marketplace. In addition, if any of our products or technology is covered by third-party patents or other intellectual property rights, we could be subject to various legal actions. We cannot assure you that our technology platform and products do not infringe patents held by others or that they will not in the future.

Litigation may be necessary to enforce our intellectual property rights, to protect our trade secrets, to determine the validity and scope of the proprietary rights of others, or to defend against claims of infringement, invalidity, misappropriation, or other claims.

Any such litigation could result in substantial costs and diversion of our resources. Moreover, any settlement of or adverse judgment resulting from litigation relating to intellectual property could require us to obtain a license to continue to make, use or sell the products or technology that is the subject of the claim, or otherwise restrict or prohibit our use of the technology.

Our ability to compete may decline if we do not adequately protect our proprietary technologies or if we lose some of our intellectual property rights.

Our success depends in part on our ability to obtain patents and maintain adequate protection of our intellectual property for our technologies and products and potential products in the United States and other countries. We have adopted a strategy of seeking patent protection in the United States and in foreign countries with respect to certain of the technologies used in or relating to our products and processes. As such, as of December 31, 2018, we owned or controlled approximately 1,100 issued patents and pending patent applications in the United States and in various foreign jurisdictions. Our intellectual property rights, as of December 31, 2018, have terms that expire between 2019 and 2039. We also have license rights to a number of issued patents and pending patent applications in the United States and in various foreign jurisdictions. Our owned and licensed patents and patent applications include those directed to our enabling technologies and to the methods and products that support our business in the pharmaceuticals manufacturing and complex chemistry markets. We intend to continue to apply for patents relating to our technologies, methods and products as we deem appropriate.

Numerous patents in our portfolio involve complex legal and factual questions and, therefore, enforceability cannot be predicted with any certainty. Issued patents and patents issuing from pending applications may be challenged, invalidated, or circumvented. Moreover, the United States Leahy-Smith America Invents Act (“AIA”), enacted in September 2011, brought significant changes to the United States patent system, which include a change to a “first to file” system from a “first to invent” system and changes to the procedures for challenging issued patents and disputing patent applications during the examination process, among other things. While interference proceedings are possible for patent claims filed prior to March 16, 2013, many of our filings will be subject to the post- and pre-grant proceedings set forth in the AIA, including citation of prior art and written statements by third parties, third party pre-issuance submissions, ex parte reexamination, inter partes review, post-grant review, and derivation proceedings. We may need to utilize the processes provided by the AIA for supplemental examination or patent reissuance. These proceedings could result in substantial cost to us even if the outcome is favorable. Even if successful, any interference may result in loss of certain claims. Any litigation or proceedings could divert our management's time and efforts. Even unsuccessful claims filed by third parties could result in significant legal fees and other expenses, diversion of management time, and disruption in our business. Uncertainties resulting from initiation and continuation of any patent or related litigation could harm our ability to compete. We have not assessed the applicability of the AIA and new regulations on our patent portfolio. These changes could increase the costs and uncertainties surrounding the prosecution of our patent applications and the enforcement or defense of our patent rights.

Additional uncertainty may result from legal precedent handed down by the United States Federal Circuit Court and Supreme Court as they determine legal issues concerning the scope and construction of patent claims and inconsistent interpretation of patent laws by the lower courts. Accordingly, we cannot ensure that any of our pending patent applications will result in issued patents, or even if issued, predict the breadth of the claims upheld in our and other companies' patents. Given that the degree of future protection for our proprietary rights is uncertain, we cannot ensure that: (i) we were the first to invent the inventions covered by each of our pending applications, (ii) we were the first to file patent applications for these inventions, or (iii) the proprietary technologies we develop will be patentable. In addition, unauthorized parties may attempt to copy or otherwise obtain and use our products or technology. Monitoring unauthorized use of our intellectual property is difficult, and we cannot be certain that the steps we have taken will prevent unauthorized use of our technology, particularly in certain foreign countries where the local laws may not protect our proprietary rights as fully as in the United States. Moreover, third parties could practice our inventions in territories where we do not have patent protection. Such third parties may then try to import products made using our inventions into the United States or other territories. If competitors are able to use our technology, our ability to compete effectively could be harmed. In addition, others may independently develop and obtain patents for technologies that are similar to or superior to our technologies. If that happens, we may need to license these

technologies, and we may not be able to obtain licenses on reasonable terms, if at all, which could cause harm to our business.

Third parties may claim that we are infringing their intellectual property rights or other proprietary rights, which may subject us to costly and time consuming litigation and prevent us from developing or commercializing our products.

Our commercial success also depends in part on our ability to operate without infringing patents and proprietary rights of third parties, and without breaching any licenses or other agreements that we have entered into with regard to our technologies, products and business. We cannot ensure that patents have not been issued to third parties that could block our ability to obtain patents or to operate as we would like. There may be patents in some countries that, if valid, may block our ability to make, use or sell our products in those countries, or import our products into those countries, if we are unsuccessful in circumventing or

acquiring rights to these patents. There also may be claims in patent applications filed in some countries that, if granted and valid, may also block our ability to commercialize products or processes in these countries if we are unable to circumvent or license them.

The industries in which we operate and the biotechnology industry, in particular, are characterized by frequent and extensive litigation regarding patents and other intellectual property rights. Many biotechnology companies have employed intellectual property litigation as a way to gain a competitive advantage. Our involvement in litigation or other intellectual property proceedings inside and outside of the United States, to defend our intellectual property rights or as a result of alleged infringement of the rights of others, may divert our management's time from focusing on business operations and could cause us to spend significant amounts of money. Any potential intellectual property litigation also could force us to do one or more of the following:

- stop selling or using our products or technologies that use the subject intellectual property;
- pay monetary damages or substantial royalties;
- grant cross-licenses to third parties relating to our patents or proprietary rights;
- obtain from the third party asserting its intellectual property rights a license to sell or use the relevant technology, which license may not be available on reasonable terms, or at all; or
- redesign those products or processes that use any allegedly infringing technology, or relocate the operations relating to the allegedly infringing technology to another jurisdiction, which may result in significant cost or delay to us, could be technically infeasible or could prevent us from selling some of our products in the United States or other jurisdictions.

We are aware of some patents and patent applications relating to aspects of our technologies filed by, and issued to, third parties. We cannot assure you that if this third party intellectual property is asserted against us that we would ultimately prevail.

We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we have in the past filed, and may in the future be required to file, infringement claims, which can be expensive and time-consuming. See Item 3, "Legal Proceedings." In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed. In legal proceedings against a third party to enforce a patent directed at one of our technologies or products, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our expenses and reduce the resources available for operations and research and development activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace. Furthermore, because of the

substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries where we do business do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual

property rights in certain foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property, particularly those relating to biotechnology and/or bioindustrial technologies. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. This could make it difficult for us to stop the infringement of our patents or misappropriation of our other intellectual property rights. Additionally, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business.

If we lose key personnel, including key management personnel, or are unable to attract and retain additional personnel as needed in the future, it could disrupt the operation of our business, delay our product development programs, harm our research and development efforts, and/or impact our ability to pursue and build collaborations.

Our business involves complex, global operations across a variety of markets and requires a management team and employee workforce that is knowledgeable in the many areas in which we operate. The loss of any key members of our management team or the failure to attract or retain other key employees who possess the requisite expertise for the conduct of our business could prevent us from developing and commercializing our products for our target markets and entering into collaborations or licensing arrangements to execute on our business strategy.

In addition, the loss of any key scientific staff, or the failure to attract or retain other key scientific employees, could prevent us from developing and commercializing our products for our target markets and entering into collaborations or licensing arrangements to execute on our business strategy. We may not be able to attract or retain qualified employees in the future due to the intense competition for qualified personnel among biotechnology and other technology-based businesses or due to the availability of personnel with the qualifications or experience necessary for our business. If we are not able to attract and retain the necessary personnel to accomplish our business objectives, we may experience staffing constraints that will adversely affect our ability to meet the demands of our collaborators and customers in a timely fashion or to support our internal research and development programs. Competition for experienced scientists and other technical personnel from numerous companies and academic and other research institutions may limit our ability to do so on acceptable terms. All of our employees are at-will employees, which mean that either the employee or we may terminate their employment at any time.

Our planned activities will require additional expertise in specific industries and areas applicable to the products and processes developed through our technology platform or acquired through strategic or other transactions, especially in the end markets that we seek to penetrate. These activities will require the addition of new personnel, and the development of additional expertise by existing personnel. The inability to attract personnel with appropriate skills or to develop the necessary expertise could impair our ability to grow our business.

If our protein catalysts, or the genes that code for our protein catalysts, are stolen, misappropriated or reverse engineered, others could use these biocatalysts or genes to produce competing products.

Third parties, including our contract manufacturers, customers and those involved in shipping our protein catalysts, often have custody or control of our protein catalysts. If our protein catalysts, or the genes that code for our protein catalysts, were stolen, misappropriated or reverse engineered, they could be used by other parties who may be able to reproduce these protein catalysts for their own commercial gain. If this were to occur, it may be difficult for us to challenge this type of use, especially in countries with limited intellectual property protection or in countries in which we do not have patents covering the misappropriated biocatalysts.

Confidentiality agreements with employees and others may not adequately prevent disclosures of trade secrets and other proprietary information.

We rely in part on trade secret protection to protect our confidential and proprietary information and processes. However, trade secrets are difficult to protect. We have taken measures to protect our trade secrets and proprietary information, but these measures may not be effective. We require employees and consultants to execute confidentiality agreements upon the commencement of an employment or consulting arrangement with us. These agreements generally require that all confidential information developed by the individual or made known to the individual by us during the course of the individual’s relationship with us be kept confidential and not disclosed to third parties. These agreements also generally provide that inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. Nevertheless, our proprietary information may be disclosed,

third parties could reverse engineer our biocatalysts and others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

We may need additional capital in the future in order to expand our business.

Our future capital requirements may be substantial, particularly as we continue to develop our business. Although we believe that, based on our current level of operations, our existing cash, cash equivalents and equity securities will provide adequate funds for ongoing operations, planned capital expenditures and working capital requirements for at least the next 12 months, we may need additional capital if our current plans and assumptions change. Our need for additional capital will depend on many factors, including the financial success of our biocatalysis business, our spending to develop and commercialize new and existing products and the amount of collaboration funding we may receive to help cover the cost of such expenditures, the effect of any acquisitions of other businesses, technologies or facilities that we may make or develop in the future, our spending on new market opportunities, including opportunities in the fine chemicals markets, and the filing, prosecution, enforcement and defense of patent claims. If our capital resources are insufficient to meet our capital requirements, and we are unable to enter into or maintain collaborations with partners that are able or willing to fund our development efforts or commercialize any products that we develop or enable, we will have to raise additional funds to continue the development of our technology and products and complete the commercialization of products, if any, resulting from our technologies. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. We may seek to obtain such additional capital through equity offerings, debt financings, credit facilities and/or strategic collaborations. If future financings involve the issuance of equity securities, our existing stockholders would suffer dilution. If we raise debt financing or enter into credit facilities, we may be subject to restrictive covenants that limit our ability to conduct our business. Strategic collaborations may also place restrictions on our business. We may not be able to raise sufficient additional funds on terms that are favorable to us, if at all. If we fail to raise sufficient funds and fail to generate sufficient revenues to achieve planned gross margins and to control operating costs, our ability to fund our operations, take advantage of strategic opportunities, develop products or technologies, or otherwise respond to competitive pressures could be significantly limited. If this happens, we may be forced to delay or terminate research or development programs or the commercialization of products resulting from our technologies, curtail or cease operations or obtain funds through collaborative and licensing arrangements that may require us to relinquish commercial rights, or grant licenses on terms that are not favorable to us. If adequate funds are not available, we will not be able to successfully execute our business plan or continue our business.

If we are unable to comply with the terms of our credit facility, our business and financial condition would be materially and adversely affected.

On June 30, 2017 we entered into a credit facility ("Credit Facility") financing arrangement secured by a lien on substantially all of our personal property other than our intellectual property. Although we have made no loans or draws under the Credit Facility as of December 31, 2018, the Credit Facility includes affirmative and negative covenants including, among others, covenants requiring us to achieve consolidated product revenues at minimum levels and restricting our ability to transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay dividends or make other distributions, make investments, create liens and sell assets. The Credit Facility also includes events of default including, among other things, our failure to pay any amounts due under the Credit Facility, a breach of covenants under the Credit Facility, our insolvency, a material adverse change, the occurrence of any default under certain other indebtedness in an amount greater than $250,000 and a final judgment against us in an amount greater than $250,000. If an event of default occurs, it could cause our obligations to become immediately due and payable and our lender would be entitled to foreclose against the collateral securing the indebtedness, including our cash. If our indebtedness were to be accelerated, we may be unable to repay such debt and, therefore, such acceleration could materially and adversely affect our business and financial condition. For more information regarding our compliance with our financial covenants, see “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

Debt service obligation may place us at a competitive disadvantage in our industry.

Draws under the Credit Facility would create debt service obligations for us. Although we have not drawn on the Credit Facility to date, any future draws under the Credit Facility and the related debt service requirements could adversely affect our ability to operate our business and may limit our ability to take advantage of potential business

opportunities. For example, the Credit Facility presents the following risks, certain of which apply regardless of whether we draw on the Credit Facility:

- we may be required to use a portion of our cash flow from operations to make debt service payments, thereby reducing the availability of our cash flow to fund working capital, capital expenditures, product development efforts, research and development, and other general corporate requirements;
- our interest expense could increase if prevailing interest rates increase, because a portion of draws which could be made under the Credit Facility bear interest at floating rates;

- the Credit Facility could reduce our flexibility to adjust to changing business conditions or obtain additional financing to fund working capital, capital expenditures, product development efforts, research and development, and other general corporate requirements; and
- restrictive covenants in our Credit Facility, which apply regardless of whether we draw down under the facility, limit our ability to, among other things, transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay dividends or make other distributions, make investments, create liens and sell assets.

Our revenues, financial condition and results of operations may also be adversely affected if one or more of our customers is delayed in paying, or becomes unable to pay, for our delivered products on a timely basis.

Certain of our customers may become subject to financial and other challenges that affect their cash flow. If these customers fail to pay us on a timely basis it may cause our financial results to fluctuate. Failure by such customers to pay us on timely basis, or at all, would adversely impact our financial condition.

If goodwill or other long-lived assets become impaired we may be required to record a significant charge to earnings.

Our total assets reflect goodwill of $3.2 million and other long-lived assets of $5.8 million as of December 31, 2018. Under accounting principles generally accepted in the United States ("GAAP"), we review goodwill for impairment on at least an annual basis and at any interim date whenever events or changes in circumstances indicate that the carrying value may not be recoverable. We review our long lived assets with finite lives for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. Events or changes in circumstances (i.e., information that indicates an impairment might exist) could include: a significant decrease in the market price of our common stock; current period cash flow losses or operating losses combined with a history of losses or a forecast of continuing losses associated with the use of the assets; slower growth rates in our industry; significant adverse changes in the business climate or legal factors; accumulation of costs significantly in excess of the amount originally expected for the acquisition or construction of the assets; loss of significant customers or partners; or the current expectation that the assets will more likely than not be sold or disposed of significantly before the end of their estimated useful life. We tested goodwill for impairment as of December 31, 2018. Based on our analysis, we determined that the fair value of goodwill at the reporting unit level exceeded their carrying value and that no impairment was necessary as of December 31, 2018. Nevertheless, we may experience additional events or changes in circumstances in the future that we determine to be indicators of impairment and that may in turn require us to undertake impairment analysis in future periods. Depending on the circumstances and judgments made at such future time, the outcome of the analysis may require us to recognize impairment.

We may be required to record a significant charge to earnings in our financial statements during the period in which any impairment of our goodwill or other long-lived assets is determined, resulting in an adverse impact on our financial position and results of operations.

Changes in financial accounting standards or practices may cause adverse, unexpected financial reporting fluctuations and affect our reported results of operations.

Financial accounting standards may change or their interpretation may change. A change in accounting standards or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change becomes effective. Changes to existing rules or the re-examining of current practices may adversely affect our reported financial results or the way we conduct our business. In particular, in order to be able to comply with the requirements of the revenue recognition standard under Accounting Standards Update (ASU) 2014-09 Revenue from Contracts with Customers (Topic 606) and related amendments ("ASC 606"), we have updated and enhanced our internal accounting processes and our internal controls over financial reporting. This has required, and will continue to require, additional investments by us, and may require incremental resources that could increase our operating costs in future periods. Further, the timing of recognition for our product sales under certain license and supply agreements and research and development revenues, on or after January 1, 2018, have been changed as a result of ASC 606.

If we are unable to maintain effective internal control over financial reporting in the future, the accuracy and timeliness of our financial reporting may be adversely affected.

Section 404 of the Sarbanes-Oxley Act of 2002 requires companies to conduct a comprehensive evaluation of their disclosure controls and procedures over financial reporting. At the end of each fiscal year, we must perform an

evaluation of our disclosure controls and procedures over financial reporting, include in our annual report the results of the evaluation, and have our external auditors publicly attest to such evaluation.

We have identified material weaknesses and other control deficiencies in the past, and while the material weaknesses have since been remediated, we cannot assure you that in the future additional material weaknesses or significant deficiencies will not exist or otherwise be discovered. If other deficiencies are discovered in the future, our ability to accurately report our financial position, results of operations or cash flows on timely basis could be impaired, which could result in late filings of our annual and quarterly reports under the Exchange Act, restatements of our consolidated financial statements, a decline in our stock price, suspension or delisting of our common stock by the Nasdaq Stock Market, or other material adverse effects on our business, reputation, results of operations, financial condition or liquidity.

We are dependent on information technology systems, infrastructure and data, and any failure of these systems could harm our business. Security breaches, loss of data, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business, results of operations and financial condition.

Information technology helps us operate efficiently, interface with customers, maintain financial accuracy and efficiency, and accurately produce our financial statements. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology infrastructure, we could be subject to transaction errors, processing inefficiencies, the loss of customers, business disruptions, or the loss of or damage to intellectual property through security breach. If our data management systems do not effectively collect, store, process, and report relevant data for the operation of our business, whether due to equipment malfunction or constraints, software deficiencies, or human error, our ability to effectively plan, forecast, and execute our business plan and comply with applicable laws and regulations will be impaired, perhaps materially. Any such impairment could materially and adversely affect our financial condition, results of operations, cash flows, and the timeliness with which we report our internal and external operating results.

Our business may require us to use and store customer, employee, and business partner personally identifiable information ("PII"). This may include names, addresses, phone numbers, email addresses, contact preferences, tax identification numbers, and payment account information. We require user names and passwords in order to access our information technology systems. We also use encryption and authentication technologies to secure the transmission and storage of data. These security measures may be compromised as a result of security breaches by unauthorized persons, employee error, malfeasance, faulty password management, or other irregularity, and result in persons obtaining unauthorized access to our data or accounts. Third parties may attempt to fraudulently induce employees or customers into disclosing user names, passwords, or other sensitive information, which may in turn be used to access our information technology systems. For example, our employees have received "phishing" emails and phone calls attempting to induce them to divulge passwords and other sensitive information.

In addition, unauthorized persons may attempt to hack into our products or systems to obtain personal data relating to employees and other individuals, our confidential or proprietary information or confidential information we hold on behalf of third parties. If the unauthorized persons successfully hack into or interfere with our connected products or services, they may create issues with product functionality that could pose a risk of loss of data. We have programs in place to detect, contain, and respond to data security incidents, and we make ongoing improvements to our information-sharing products in order to minimize vulnerabilities, in accordance with industry and regulatory standards. However, because the techniques used to obtain unauthorized access to or sabotage systems change frequently and may be difficult to detect, we may not be able to anticipate and prevent these intrusions or mitigate them when and if they occur.

We also rely on external vendors to supply and/or support certain aspects of our information technology systems. The systems of these external vendors may contain defects in design or manufacture or other problems that could unexpectedly compromise information security of our own systems, and we are dependent on these third parties to deploy appropriate security programs to protect their systems.

While we devote significant resources to network security, data encryption, and other security measures to protect our systems and data, these security measures cannot provide absolute security. We may experience a breach of our systems and may be unable to protect sensitive data. The costs to us to eliminate or alleviate network security problems, bugs, viruses, worms, malicious software programs, and security vulnerabilities could be significant. Our

efforts to address these problems may not be successful and could result in unexpected interruptions, delays, cessation of service, and harm to our business operations. Moreover, if a computer security breach affects our systems or results in the unauthorized release of PII, our reputation and brand could be materially damaged and use of our products and services could decrease. We would also be exposed to a risk of loss or litigation and potential liability, which could have a material adverse impact on our business, financial condition, results of operations, or cash flows.

Our business is subject to complex and evolving laws and regulations regarding privacy, data protection and other matters relating to information collection.

There are numerous state, federal and foreign laws, regulations, decisions, and directives regarding privacy and the collection, storage, transmission, use, processing, disclosure and protection of PII and other personal, customer, or other data, the scope of which is continually evolving and subject to differing interpretations. We may be subject to significant consequences, including penalties and fines, for any failure to comply with such laws, regulations and directives.

Furthermore, any failure, or perceived failure, by us to comply with or make effective modifications to our policies, or to comply with any federal, state or international privacy, data-retention or data-protection-related laws, regulations, orders or industry self-regulatory principles could result in proceedings or actions against us by governmental entities or others, a loss of customer confidence, damage to our brand and reputation and a loss of customers, any of which could have an adverse effect on our business. In addition, various federal, state and foreign legislative or regulatory bodies may enact new or additional laws and regulations concerning privacy, data-retention and data-protection issues, including laws or regulations mandating disclosure to domestic or international law enforcement bodies, which could adversely impact our business or our reputation with customers. For example, some countries have adopted laws mandating that some PII regarding customers in their country be maintained solely in their country. Having to maintain local data centers and redesign product, service and business operations to limit PII processing to within individual countries could increase our operating costs significantly.

Our product gross margins are variable and may decline from quarter to quarter.

Our product gross margins have varied significantly in the past and may continue to fluctuate from quarter to quarter and year to year in the future due to a variety of factors, including product mix, pricing pressure from our pharmaceutical customers and competition from other products or technologies. This variability may have a material adverse impact on our operating results and financial condition and cause our stock price to decline.

We face risks associated with our international business.

While we have a limited number of employees located outside of the United States, we are and will continue to be dependent upon contract manufacturers located outside of the United States. In addition, we have customers and partners located outside of the United States. Conducting business internationally exposes us to a variety of risks, including:

- changes in or interpretations of foreign regulations that may adversely affect our ability to sell our products, repatriate profits to the United States or operate our foreign-located facilities;
- the imposition of tariffs;
- the imposition of limitations on, or increase of, withholding and other taxes on remittances and other payments by foreign subsidiaries or joint ventures;
- the imposition of limitations on genetically-engineered products or processes and the production or sale of those products or processes in foreign countries;
- currency exchange rate fluctuations;
- uncertainties relating to foreign laws, regulations and legal proceedings including tax, import/export, anti-corruption and exchange control laws;
- the availability of government subsidies or other incentives that benefit competitors in their local markets that are not available to us;
- increased demands on our limited resources created by our operations may constrain the capabilities of our administrative and operational resources and restrict our ability to attract, train, manage and retain qualified management, technicians, scientists and other personnel;
- economic or political instability in foreign countries;
- difficulties associated with staffing and managing foreign operations; and
- the need to comply with a variety of United States and foreign laws applicable to the conduct of international business, including import and export control laws and anti-corruption laws.

Compliance with European Union chemical regulations could be costly and adversely affect our business and results of operations.

Some of our products are subject to the European Union regulatory regime known as The Registration, Evaluation and Authorization of Chemicals ("REACH"). REACH mandates that certain chemicals manufactured in, or imported into, the European Union be registered and evaluated for their potential effects on human health and the environment. Under REACH, we and our contract manufacturers located in the European Union are required to register certain of our products based on the quantity of such product imported into or manufactured in the European Union and on the product's intended end-use. The registration, evaluation and authorization process under REACH can be costly and time consuming. Problems or delays in the registration, evaluation or authorization process under REACH could delay or prevent the manufacture of some of our products in, or the importation of some of our products into, the European Union, which could adversely affect our business and results of operations. In addition, if we or our contract manufacturers fail to comply with REACH, we may be subject to penalties or other enforcement actions, which could have a material adverse effect on our business and results of operations.

Competitors and potential competitors who have greater resources and experience than we do may develop products and technologies that make ours obsolete or may use their greater resources to gain market share at our expense.

The biocatalysis industry and each of our target markets are characterized by rapid technological change. Our future success will depend on our ability to maintain a competitive position with respect to technological advances. In addition, as we enter new markets, we will face new competition and will need to adapt to competitive factors that may be different from those we face today.

We are aware that other companies, including Royal DSM, N.V. ("DSM"), BASF, and Novozymes have alternative methods for obtaining and generating genetic diversity or use mutagenesis techniques to produce genetic diversity. Academic institutions such as the California Institute of Technology, the Max Planck Institute and the Austrian Centre of Industrial Biotechnology are also working in this field. Technological development by others may result in our products and technologies, as well as products developed by our customers using our biocatalysts, becoming obsolete.

Our primary competitors in the biocatalysis for pharmaceutical products are companies marketing either conventional, non-enzymatic processes or biocatalytic enzymes to manufacturers of pharmaceutical intermediates and APIs, and also existing in-house technologies (both biocatalysts and conventional catalysts) within our client and potential client companies. The principal methods of competition and competitive differentiation in this market are price, product quality and performance, including manufacturing yield, safety and environmental benefits, and speed of delivery of product. Pharmaceutical manufacturers that use biocatalytic processes can face increased competition from manufacturers that use more conventional processes and/or manufacturers that are based in regions (such as India and China) with lower regulatory, safety and environmental costs.

The market for the manufacture and supply of APIs and intermediates is large with many established companies. These companies include many of our large innovator and generic pharmaceutical customers, such as Merck, GSK, Pfizer, Bristol Myers, Squibb and Teva Pharmaceutical Industries Ltd., which have significant internal research and development efforts directed at developing processes to manufacture APIs and intermediates. The processes used by these companies include classical conventional organic chemistry reactions, chemo catalytic reactions, biocatalytic reactions or combinations thereof. Our biocatalytic based manufacturing processes must compete with these internally developed routes. Additionally, we also face competition from companies developing and marketing conventional catalysts such as Solvias Inc., BASF and Takasago International Corporation.

The market for supplying enzymes for use in pharmaceutical manufacturing is quite fragmented. There is competition from large industrial enzyme companies, such as Novozymes, as well as subsidiaries of larger CRO/CMOs, such as DSM, Cambrex Corporation and Almac Group Ltd. There is also competition in the customized and optimized enzyme area from several smaller companies, such as BRAIN AG, Arzeda, c-LEcta GmbH, Gingko Bioworks, Zymergen, and Evocatal GmbH.

We entered the fine chemicals market in 2013, by applying our protein engineering technology in the food market. We face similar forms of competition in this market as in the pharmaceutical markets with the exception that the risk of losing opportunities to larger competitors in fine chemicals is greater given the larger scale of opportunities available in the fine chemicals market compared to the pharmaceutical market. Our significant competitors in the fine chemicals

markets include companies that have been in these marketplaces for many years, such as DuPont Industrial Biosciences (DuPont Genencor), DSM, Novozymes and A.B. Enzymes. These companies have greater resources in these markets than we do and have long-term supply arrangements already in place with customers. Our ability to compete in these markets may be limited by our relatively late entrance. We also face competition in both the fine chemicals and pharmaceutical markets from emerging companies offering whole cell metabolic pathway approaches to these markets.

There are numerous companies that participate in the biotherapeutics market generally and the PKU market specifically. Many of these companies are large, successful and well-capitalized. BioMarin Pharmaceutical Inc. ("BioMarin") and Daiichi Sankyo Company market Kuvan® in the United States, Europe and Japan for the treatment of a certain type of PKU. In addition, BioMarin gained US FDA approval in 2018 and began commercial sales of Palynziq™ as an injectable enzyme substitution therapy for the potential treatment of PKU. Synlogic is developing SYNB1618 as a potential treatment for PKU, and in 2018, they completed a phase 1/2a clinical trial using SYNB1618. Takeda (who recently acquired Shire Plc), Genzyme / Sanofi S.A. and other companies market or are actively developing new enzyme therapeutics. There are numerous companies that are developing other forms of therapeutics, such as small molecules and gene therapies, which could compete with biotherapeutics.

Our ability to compete successfully in any of these markets will depend on our ability to develop proprietary products that reach the market in a timely manner and are technologically superior to and/or are less expensive than other products on the market. Many of our competitors have substantially greater production, financial, research and development, personnel and marketing resources than we do. They also started developing products earlier than we did, which may allow them to establish blocking intellectual property positions or bring products to market before we can. In addition, certain of our competitors may also benefit from local government subsidies and other incentives that are not available to us. As a result, our competitors may be able to develop competing and/or superior technologies and processes, and compete more aggressively and sustain that competition over a longer period of time than we could. Our technologies and products may be rendered obsolete or uneconomical by technological advances or entirely different approaches developed by one or more of our competitors. We cannot be certain that any products we develop in the future will compare favorably to products offered by our competitors or that our existing or future products will compare favorably to any new products that are developed by our competitors. As more companies develop new intellectual property in our markets, the possibility of a competitor acquiring patent or other rights that may limit our products or potential products increases, which could lead to litigation.

Our limited resources relative to many of our competitors may cause us to fail to anticipate or respond adequately to new developments and other competitive pressures. This failure could reduce our competitiveness and market share, adversely affect our results of operations and financial position, and prevent us from obtaining or maintaining profitability.

We must rely on our suppliers, contract manufacturers and customers to deliver timely and accurate information in order to accurately report our financial results in the time frame and manner required by law.

We need to receive timely, accurate and complete information from a number of third parties in order to accurately report our financial results on a timely basis. We rely on suppliers and certain contract manufacturers to provide us with timely and accurate information regarding our inventories and manufacturing cost information, and we rely on current and former collaborators to provide us with product sales and cost saving information in connection with royalties owed to us. Any failure to receive timely information from one or more of these third parties could require that we estimate a greater portion of our revenues and other operating performance metrics for the period, which could cause our reported financial results to be incorrect. Moreover, if the information that we receive is not accurate, our financial statements may be materially incorrect and may require restatement, and we may not receive the full amount of revenues that we are entitled to under these arrangements. Although we typically have audit rights with these parties, performing such an audit could be harmful to our collaborative relationships, expensive and time consuming and may not be sufficient to reveal any discrepancies in a timeframe consistent with our reporting requirements.

Our results of operations may be adversely affected by the results of regulatory tax examinations.

We are subject to value added tax, customs tax, sales and use tax, withholding tax, payroll tax, income tax and other taxes in connection with the operation of our business. Regulators from the various jurisdictions in which we operate periodically perform audits, and we are regularly subject to, and are currently undergoing, audits and assessments by tax authorities in the United States and foreign jurisdictions for prior tax years. Although we believe our tax estimates are reasonable, and we intend to defend our positions if necessary, the final outcome of tax audits and related proceedings is inherently uncertain and could be materially different than that reflected in our historical income tax provisions and accruals. Moreover, we could be subject to assessments of substantial additional taxes and/or fines or penalties relating to ongoing or future audits. The adverse resolution of any audits or related proceedings could have

an adverse effect on our financial position and results of operations.

Business interruptions could delay us in the process of developing our products and could disrupt our sales.

Our headquarters is located in the San Francisco Bay Area near known earthquake fault zones and is vulnerable to significant damage from earthquakes. We are also vulnerable to other types of natural disasters and other events that could disrupt our operations, such as riot, civil disturbances, war, terrorist acts, flood, infections in our laboratory or production facilities or those of our contract manufacturers and other events beyond our control. We do not carry insurance for earthquakes and we may not

carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our cash flows and success as an overall business.

Ethical, legal and social concerns about genetically engineered products and processes could limit or prevent the use of our products, processes, and technologies and limit our revenues.

Some of our products and processes are genetically engineered or involve the use of genetically engineered products or genetic engineering technologies. If we and/or our collaborators are not able to overcome the ethical, legal, and social concerns relating to genetic engineering, our products and processes may not be accepted. Any of the risks discussed below could result in increased expenses, delays, or other impediments to our programs or the public acceptance and commercialization of products and processes dependent on our technologies or inventions. Our ability to develop and commercialize one or more of our technologies, products, or processes could be limited by the following factors:

- public attitudes about the safety and environmental hazards of, and ethical concerns over, genetic research and genetically engineered products and processes, which could influence public acceptance of our technologies, products and processes;
- public attitudes regarding, and potential changes to laws governing ownership of genetic material, which could harm our intellectual property rights with respect to our genetic material and discourage collaborators from supporting, developing, or commercializing our products, processes and technologies; and
- governmental reaction to negative publicity concerning genetically modified organisms, which could result in greater government regulation of genetic research and derivative products. The subject of genetically modified organisms has received negative publicity, which has aroused public debate. This adverse publicity could lead to greater regulation and trade restrictions on imports of genetically altered products. The protein catalysts that we develop have significantly enhanced characteristics compared to those found in naturally occurring enzymes or microbes. While we produce our biocatalysts only for use in a controlled industrial environment, the release of such biocatalysts into uncontrolled environments could have unintended consequences. Any adverse effect resulting from such a release could have a material adverse effect on our business and financial condition, and we may have exposure to liability for any resulting harm.

If we engage in any acquisitions, we will incur a variety of costs and may potentially face numerous risks that could adversely affect our business and operations.

We have made acquisitions in the past, and if appropriate opportunities become available, we expect to acquire additional businesses, assets, technologies, or products to enhance our business in the future. For example, in October 2010, we acquired substantially all of the patents and other intellectual property rights associated with Maxygen's directed evolution technology.

In connection with any future acquisitions, we could:

- issue additional equity securities, which would dilute our current stockholders;
- incur substantial debt to fund the acquisitions;
- use our cash to fund the acquisitions; or
- assume significant liabilities including litigation risk.

Acquisitions involve numerous risks, including problems integrating the purchased operations, technologies or products, unanticipated costs and other liabilities, diversion of management's attention from our core businesses, adverse effects on existing business relationships with current and/or prospective collaborators, customers and/or suppliers, risks associated with entering markets in which we have no or limited prior experience and potential loss of key employees. We do not have extensive experience in managing the integration process and we may not be able to successfully integrate any businesses, assets, products, technologies, or personnel that we might acquire in the future without a significant expenditure of operating, financial and management resources, if at all. The integration process could divert management's time from focusing on operating our business, result in a decline in employee morale and cause retention issues to arise from changes in compensation, reporting relationships, future prospects or the direction of the business. Acquisitions may also require us to record goodwill and non-amortizable intangible assets that will be subject to impairment testing on a regular basis and potential periodic impairment charges, incur amortization expenses related to certain intangible assets, and incur large and immediate write offs and restructuring and other

related expenses, all of which could harm our operating results and financial condition. In addition, we may acquire companies that have insufficient internal financial controls, which could impair our ability to integrate the acquired company and adversely impact our financial reporting. If we fail in our integration efforts with respect to any of our acquisitions and are unable to efficiently operate as a combined organization, our business and financial condition may be adversely affected.

We use hazardous materials in our business and we must comply with environmental laws and regulations. Any claims relating to improper handling, storage or disposal of these materials or noncompliance of applicable laws and regulations could be time consuming and costly and could adversely affect our business and results of operations.

Our research and development and commercial processes involve the use of hazardous materials, including chemical, radioactive, and biological materials. Our operations also produce hazardous waste. We cannot eliminate entirely the risk of accidental contamination or discharge and any resultant injury from these materials. Federal, state, local and foreign laws and regulations govern the use, manufacture, storage, handling and disposal of, and human exposure to, these materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our total assets. Although we believe that our activities comply in all material respects with environmental laws, there can be no assurance that violations of environmental, health and safety laws will not occur in the future as a result of human error, accident, equipment failure or other causes.

Compliance with applicable environmental laws and regulations may be expensive, and the failure to comply with past, present, or future laws could result in the imposition of fines, third party property damage, product liability and personal injury claims, investigation and remediation costs, the suspension of production, or a cessation of operations, and our liability may exceed our total assets. Liability under environmental laws can be joint and several and without regard to comparative fault. Environmental laws could become more stringent over time imposing greater compliance costs and increasing risks and penalties associated with violations, which could impair our research, development or production efforts and harm our business. In addition, we may have to indemnify some of our customers or suppliers for losses related to our failure to comply with environmental laws, which could expose us to significant liabilities.

We may be sued for product liability.

The design, development, manufacture and sale of our products involve an inherent risk of product liability claims and the associated adverse publicity. For example, we may be named directly in product liability suits relating to drugs that are produced using our enzymes or that incorporate our intermediates and APIs. The biocatalysts, pharmaceutical intermediates and APIs that we produce or are produced for us by our manufacturing partners could be subject to quality control or contamination issues of which we are not aware. Claims could be brought by various parties, including customers who are purchasing products directly from us, other companies who purchase products from our customers or by the end users of the drugs. We could also be named as co-parties in product liability suits that are brought against our contract manufacturers who manufacture our enzymes, pharmaceutical intermediates and APIs.

Insurance coverage is expensive and may be difficult to obtain, and may not be available in the future on acceptable terms, or at all. We cannot assure you that any contract manufacturer that we have used in the past or shall use in the future has or will have adequate insurance coverage to cover against potential claims. In addition, although we currently maintain product liability insurance for our products in amounts we believe to be commercially reasonable, if the coverage limits of these insurance policies are not adequate, a claim brought against us, whether covered by insurance or not, could have a material adverse effect on our business, results of operations, financial condition and cash flows. This insurance may not provide adequate coverage against potential losses, and if claims or losses exceed our liability insurance coverage, we may go out of business. Moreover, we have agreed to indemnify some of our customers for certain claims that may arise out of the use of our products, which could expose us to significant liabilities.

Uncertainties in the interpretation and application of the 2017 Tax Cuts and Jobs Act could materially affect our tax obligations and effective tax rate.

The 2017 Tax Cuts and Jobs Act (the “Tax Act”) was enacted on December 22, 2017, and significantly changed how the U.S. imposes income tax on multinational corporations. Changes include, but are not limited to, a corporate tax rate decrease from 35% to 21% effective for tax years beginning after December 31, 2017, the transition of U.S. international taxation from a worldwide tax system to a partially territorial system, and a one-time transition tax on the mandatory deemed repatriation of accumulated foreign earnings as of December 31, 2017. The U.S. Department of Treasury (“Treasury”) has broad authority to issue regulations and interpretative guidance that may significantly impact how we will apply the law and impact our results of operations in the period issued. The Tax Act requires complex computations not previously required under U.S. tax law. As of December 31, 2018, the application of accounting guidance for some of these items is still currently uncertain, as Treasury has yet to issue proposed or final regulations

for many provisions of the Act. Further, compliance with the Tax Act and the accounting for such provisions require accumulation of information not previously required or regularly produced. As additional regulatory guidance is issued by the applicable taxing authorities, as accounting treatment is clarified, and as we perform additional analysis on the application of the law, our results may be different from our current amounts, which could materially affect our tax obligations and effective tax rate.

Our ability to use our net operating loss carryforwards to offset future taxable income may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating loss carryforwards ("NOLs"), to offset future taxable income. If the Internal Revenue Service challenges our analysis that our existing NOLs are not subject to limitations arising from previous ownership changes, our ability to utilize NOLs could be limited by Section 382 of the Code. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Section 382 of the Code. Furthermore, our ability to utilize NOLs of companies that we may acquire in the future may be subject to limitations. For these reasons, we may not be able to utilize a material portion of the NOLs reflected in our financial statements, even if we attain profitability.

Risks Related to Owning our Common Stock

We are subject to anti-takeover provisions in our certificate of incorporation and bylaws and under Delaware law that could delay or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders.

Provisions in our amended and restated certificate of incorporation and our bylaws may delay or prevent an acquisition of us. Among other things, our amended and restated certificate of incorporation and bylaws provide for a board of directors which is divided into three classes, with staggered three-year terms and provide that all stockholder action must be effected at a duly called meeting of the stockholders and not by a consent in writing, and further provide that only our board of directors, the chairman of the board of directors, our chief executive officer or president may call a special meeting of the stockholders. In addition, our amended and restated certificate of incorporation allows our board of directors, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These provisions may also frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, who are responsible for appointing the members of our management team. Furthermore, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law which prohibits, with some exceptions, stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Finally, our charter documents establish advanced notice requirements for nominations for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings. Although we believe these provisions together provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer to acquire our company may be considered beneficial by some stockholders.

Concentration of ownership among our existing officers, directors and principal stockholders may prevent other stockholders from influencing significant corporate decisions and depress our stock price.

Based on the number of shares outstanding as of December 31, 2018, our officers, directors and stockholders who hold at least 5% of our stock together beneficially own approximately 40% of our outstanding common stock. If these officers, directors, and principal stockholders or a group of our principal stockholders act together, they will be able to exert a significant degree of influence over our management and affairs and control matters requiring stockholder approval, including the election of directors and approval of mergers or other business combination transactions. The interests of this concentration of ownership may not always coincide with our interests or the interests of other stockholders. For instance, officers, directors, and principal stockholders, acting together, could cause us to enter into transactions or agreements that we would not otherwise consider. Similarly, this concentration of ownership may have the effect of delaying or preventing a change in control of our company otherwise favored by our other stockholders. As of December 31, 2018, one stockholder beneficially owned approximately 12% of our common stock.

Our share price may be volatile which may cause the value of our common stock to decline and subject us to securities class action litigation.

The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- actual or anticipated fluctuations in our financial condition and operating results;

- the position of our cash, cash equivalents and equity securities;
- actual or anticipated changes in our growth rate relative to our competitors;
- actual or anticipated fluctuations in our competitors' operating results or changes in their growth rate;
- announcements of technological innovations by us, our collaborators or our competitors;

- announcements by us, our collaborators or our competitors of significant acquisitions or dispositions, strategic partnerships, joint ventures or capital commitments;
- additions or losses of one or more significant pharmaceutical products;
- announcements or developments regarding pharmaceutical products manufactured using our protein catalysts and intermediates;
- the entry into, modification or termination of collaborative arrangements;
- additions or losses of customers;
- additions or departures of key management or scientific personnel;
- competition from existing products or new products that may emerge;
- issuance of new or updated research reports by securities or industry analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- disputes or other developments related to proprietary rights, including patent litigation and our ability to obtain patent protection for our technologies;
- contractual disputes or litigation with our partners, customers or suppliers;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- general market conditions in our industry; and
- general economic and market conditions, including the recent financial crisis.

Furthermore, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of shares of our common stock. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

We may incur losses associated with currency fluctuations and may not be able to effectively hedge our exposure.

Our operating results and cash flows are subject to volatility due to fluctuations in foreign currency exchange rates. Our primary exposure to fluctuations in foreign currency exchange rates relates to cash denominated in currencies other than the U.S. dollar. The weakening of foreign currencies relative to the United States dollar adversely affects our foreign currency-denominated cash. In periods when the United States dollar declines in value as compared to the foreign currencies in which we incur expenses, our foreign-currency based cash decrease when translated into United States dollars. Conversely, the strengthening of foreign currencies relative to the United States dollar will generally be beneficial to our foreign currency-denominated cash when translated into United States dollars.

The effect of a 10% unfavorable change in exchange rates on foreign denominated receivables and cash as of December 31, 2018 would have had foreign exchange losses of approximately $0.1 million recognized as a component of other expense in our consolidated statement of operations.

We do not engage in foreign currency hedging transactions, and as a result, unfavorable movements in foreign currency exchange rates may have an adverse financial impact, which could materially adversely affect our financial condition or results of operations. See "Item 7A. Quantitative and Qualitative Disclosures About Market Risk" for additional discussion on the impact of foreign exchange risk.

If securities or industry analysts do not publish research or reports about our business, or publish negative reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. If one or more of the analysts who cover us downgrade our stock or change their opinion of our stock in a negative manner, our stock price would likely decline. If one or

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more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act and the Dodd-Frank Wall Street Reform and Consumer Protection Act, as well as related rules implemented by the Securities and Exchange Commission and the Nasdaq Stock Market, impose various requirements on public companies that require our management and other personnel to devote a substantial amount of time to compliance initiatives.

In addition, the Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management and our independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. Our compliance with Section 404 requires that we incur substantial accounting expense and expend significant management time on compliance-related issues. Moreover, if we are not able to maintain compliance with the requirements of Section 404, our stock price could decline, and we could face sanctions, delisting or investigations by the Nasdaq Global Market, or other material adverse effects on our business, reputation, results of operations, financial condition or liquidity.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Facilities

Our headquarters are located in Redwood City, California, where we lease approximately 107,200 square feet of office and laboratory space.

Our lease (“Lease”) with Metropolitan Life Insurance Company (“MetLife”) includes approximately 28,200 square feet of space located at 200 and 220 Penobscot Drive, Redwood City, California (the “Penobscot Space”), approximately 37,900 square feet of space located at 400 Penobscot Drive, Redwood City, California (the “Building 2 Space”), approximately 11,200 square feet of space located at 501 Chesapeake Drive, Redwood City, California (“501 Chesapeake Space”), and approximately 29,900 square feet of space located at 101 Saginaw Drive, Redwood City, California (the “Saginaw Space”). Through December 31, 2018, there have been seven amendments to the Lease. Through November 30, 2019, we will continue to sublease approximately 26,500 square feet of the Saginaw Space to a subtenant and we will continue to sublease approximately 13,000 square feet of the Penobscot Space to a different subtenant.

In January 2019, we entered into an Eighth Amendment to the Lease (the “Eighth Amendment”) with MetLife with respect to the Penobscot Space, the Building 2 Space and the 501 Chesapeake Space to extend the term of the Lease for additional periods. Pursuant to the Eighth Amendment, the term of the lease of the Penobscot Space and the Building 2 Space has been extended through May 2027. The lease term for 501 Chesapeake Space has been extended to May 2029. We have two consecutive options to extend the term of the lease for the Penobscot Space, the Building 2 Space and 501 Chesapeake Space for an additional period of five years per option. Our lease on the Saginaw Space will expire on January 30, 2020.

We believe that the facilities that we currently lease in California are adequate for our needs for the immediate future and that, should it be needed, additional space can be leased to accommodate any future growth.

ITEM 3. LEGAL PROCEEDINGS

We are not currently a party to any material pending litigation or other material legal proceedings.

In February 2018, we and EnzymeWorks, Inc. (U.S.), Suzhou Hanmei Biotechnology Co. Ltd, d/b/a EnzymeWorks, Inc. (China) (collectively, "EnzymeWorks"), Junhua Tao, and Andrew Tao reached a settlement concerning the lawsuit filed by us in February 2016 against EnzymeWorks, Junhua Tao, and Andrew Tao in the United States District Court for the Northern District of California. The parties have entered into a settlement agreement, the terms of which

are confidential. The parties have also

stipulated to a judgment of patent infringement of all asserted patents against EnzymeWorks, and a permanent injunction barring any future infringement. The remaining claims against EnzymeWorks, and all claims against Junhua Tao, and Andrew Tao including trade secret misappropriation, breach of contract and voidable transfer have been dismissed with prejudice. EnzymeWorks appealed the sanctions levied against them by Judge Orrick to the Federal Circuit and filed its opening brief on May 30, 2018. On July 9, 2018, Codexis filed its response brief, and EnzymeWorks filed its reply on July 30, 2018. On February 8, 2019, the Federal Circuit panel of judges assigned to the case issued an opinion affirming the lower court's ruling and remanding the case to the lower court on jurisdictional grounds to vacate the order to which the parties had earlier stipulated.

ITEM 4. MINE SAFETY DISCLOSURES
Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock is quoted on the Nasdaq Global Select Market ("Nasdaq"), under the symbol "CDXS." The following table sets forth the high and low sales prices per share of the common stock as reported on Nasdaq. Such quotations represent inter dealer prices without retail markup, markdown or commission and may not necessarily represent actual transactions.

Fiscal 2018	High	Low
First Quarter	$13.60	$7.95
Second Quarter	16.80	9.30
Third Quarter	19.60	12.85
Fourth Quarter	23.05	14.05

Fiscal 2017	High	Low
First Quarter	$5.29	$3.60
Second Quarter	5.45	3.95
Third Quarter	6.70	4.80
Fourth Quarter	8.55	5.70

As of February 22, 2019, there were approximately 132 stockholders of record. A substantially greater number of stockholders may be "street name" or beneficial holders, whose shares are held of record by banks, brokers and other financial institutions.

Stock Price Performance Graph

The following tabular information and graph compare our total common stock return with the total return for (i) the Nasdaq Composite Index and (ii) the Nasdaq Biotechnology Index for the period December 31, 2013 through December 31, 2018. The figures represented below assume an investment of $100 in our common stock at the closing price on December 31, 2013 and in the Nasdaq Composite Index and the Nasdaq Biotechnology Index on December 31, 2013 and the reinvestment of dividends into shares of common stock. The comparisons in the table and graph are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock. The tabular information and graph shall not be deemed "soliciting material" or to be "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act or the Exchange Act.

		December 31,					
$100 investment in stock or index	Ticker	2013	2014	2015	2016	2017	2018
Codexis, Inc.	CDXS	$100.00	$180.00	$302.14	$328.57	$596.43	$1,192.86
Nasdaq Composite Total Return	XCMP	$100.00	$114.75	$122.74	$133.62	$173.22	$168.30
Nasdaq Biotechnology (Total Return) Index	XNBI	$100.00	$136.28	$152.32	$119.80	$145.71	$132.80

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ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data should be read together with our consolidated financial statements and accompanying notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data in this section is not intended to replace our consolidated financial statements and the accompanying notes. Our historical results are not necessarily indicative of our future results.

We derived the consolidated statements of operations data for the fiscal years ended December 31, 2018, 2017, and 2016 and the consolidated balance sheets data as of December 31, 2018 and 2017 from our audited consolidated financial statements appearing elsewhere in this filing. The consolidated statements of operations data for the fiscal years ended December 31, 2015 and 2014 and the consolidated balance sheets data as of December 31, 2016, 2015 and 2014 have been derived from our audited consolidated financial statements not included in this filing. The data should be read in conjunction with the consolidated financial statements, related notes, and other financial information included herein.

SELECTED CONSOLIDATED FINANCIAL DATA

	Year Ended December 31,				
	2018 [1]	2017	2016	2015	2014
	(In Thousands, Except Per Share Amounts)				
Consolidated Statements of Operations Data:					
Revenues:					
Product revenue	$25,590	$26,685	$15,321	$11,376	$13,064
Research and development revenue	35,004	23,339	33,516	30,428	22,243
Total revenues	60,594	50,024	48,837	41,804	35,307
Costs and operating expenses:					
Cost of product revenue	12,620	14,327	9,753	6,586	9,726
Research and development	29,978	29,659	22,229	20,673	22,755
Selling, general and administrative	29,291	29,008	25,419	22,315	21,937
Total costs and operating expenses	71,889	72,994	57,401	49,574	54,418
Loss from operations	(11,295)	(22,970)	(8,564)	(7,770)	(19,111)
Interest income	671	147	60	19	18
Other expenses, net	(291)	(92)	(94)	(168)	(234)
Loss before income taxes	(10,915)	(22,915)	(8,598)	(7,919)	(19,327)
Provision for (benefit from) income taxes	(37)	81	(40)	(338)	(256)
Net loss	$(10,878)	$(22,996)	$(8,558)	$(7,581)	$(19,071)
Net loss per share, basic and diluted	$(0.21)	$(0.50)	$(0.21)	$(0.19)	$(0.50)
Weighted average common shares used in computing net loss per share, basic and diluted	52,205	46,228	40,629	39,438	38,209

(1) Financial results for year ended December 31, 2018, as compared to the years ended December 31, 2017, 2016, 2015, and 2014 reflect the effects of adopting ASU 2014-09, "Revenue from Contracts with Customers (Topic 606)" and the related amendments (ASC 606), which provided a new basis of accounting for our revenue arrangements during fiscal year 2018. The adoption of ASC 606 limits the comparability of revenue and certain expenses, including revenues and costs and operating expenses, presented in the results of operations for the year ended December 31, 2018 when compared to the years ended December 31, 2017, 2016, 2015, and 2014. For additional information regarding the impact from adoption of this accounting standard, see Note 3, "Revenue Recognition" to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

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	December 31,				
	2018	2017	2016	2015	2014
Consolidated Balance Sheets Data:	(In Thousands)				
Cash, cash equivalents and restricted cash	$54,485	$32,776	$20,864	$24,060	$27,198
Working capital	50,085	20,087	14,860	17,998	19,272
Total assets	79,283	53,625	35,648	44,647	48,122
Total liabilities	22,977	29,078	16,549	21,768	21,811
Total stockholders' equity	56,306	24,547	19,099	22,879	26,311

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF
FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read in conjunction with our audited consolidated financial statements and the related notes that appear elsewhere in this Annual Report on Form 10-K. This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 21E of the Exchange Act. These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "estimate," or "continue," and similar expressions or variations. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section titled "Risk Factors," set forth in Part I, Item 1A of this Annual Report on Form 10-K and elsewhere in this report. The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

Business Overview

We discover, develop and sell proteins that deliver value to our clients in a growing set of industries. We view proteins as a vast untapped source of value-creating materials, and we are using our proven technologies, which we have been continuously improving over our sixteen year history, to commercialize an increasing number of novel proteins, both as proprietary Codexis products and in partnership with our customers.

We are a pioneer in the harnessing of computational technologies to drive biology advancements. Since our inception in 2002, we have made substantial investments in the development of our CodeEvolver® protein engineering technology platform, the primary source of our competitive advantage. Our technology platform is powered by proprietary, artificial intelligence-based, computational algorithms that rapidly mine our large and continuously growing library of protein variants' performance attributes. These computational outputs enable increasingly reliable predictions for next generation protein variants to be engineered, enabling delivery of targeted performance enhancements in a time-efficient manner. In addition to its computational prowess, our CodeEvolver® protein engineering technology platform integrates additional modular competencies, including robotic high-throughput screening and genomic sequencing, organic chemistry and process development which are all coordinated to create our novel protein innovations.

Our approach to developing commercially viable biocatalytic manufacturing processes begins by conceptually designing the most cost-effective and practical process for a targeted product. We then develop optimized protein catalysts to enable that process design using our CodeEvolver® protein engineering platform technology. Engineered protein catalyst candidates - many thousands for each protein engineering project - are then rapidly screened and validated in high throughput screening under relevant manufacturing operating conditions. This approach results in an optimized protein catalyst enabling cost-efficient processes that typically are relatively simple to run in conventional manufacturing equipment. This also allows for the efficient technical transfer of our process to our manufacturing partners.

The successful embodiment of our CodeEvolver® protein engineering technology platform in commercial manufacturing processes requires well-integrated expertise in a number of technical disciplines. In addition to those directly involved in practicing our CodeEvolver® protein engineering platform technology, such as molecular biology, enzymology, microbiology, cellular engineering, metabolic engineering, bioinformatics, biochemistry and high throughput analytical chemistry, our process development projects also involve integrated expertise in organic chemistry, chemical process development, chemical engineering, fermentation process development and fermentation engineering. Our integrated, multi-disciplinary approach to biocatalyst and process development is a critical success factor for our company.

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the pharmaceuticals market, which remains our primary business focus. Our customers, which include several large global

pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development.

We have also used the technology to develop protein catalysts for use in the fine chemicals market. The fine chemicals market consists of several large market verticals, including food and food ingredients, animal feed, flavors, fragrances and agricultural chemicals.

We have also begun using the CodeEvolver® protein engineering technology platform to develop early stage, novel biotherapeutic product candidates, both for our customers and for our own business, most notably our lead program for the

potential treatment of phenylketonuria ("PKU") in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we entered into a Global Development, Option and License Agreement (the "Nestlé Agreement") with Nestec Ltd. ("Nestlé Health Science"), to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license to develop and commercialize CDX-6114. See Note 16, “Subsequent Events” in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details.

In April 2018, we entered into a strategic agreement (the "Porton Agreement") with Porton Pharma Solutions, Ltd. ("Porton") to license key elements of our platform technology to Porton’s global custom intermediate and active pharmaceutical ingredients ("API") development and manufacturing business. This gives us access to a wide variety of small and medium-sized pharmaceutical customers.

We are also using our technology to develop enzymes for customers using next generation sequencing ("NGS") and polymerase chain reaction ("PCR/qPCR") for in vitro molecular diagnostic and genomic research applications. Our first enzyme is a ligase which we began marketing to customers in 2018.

Business Segments

We manage our business as two business segments: Performance Enzymes and Novel Biotherapeutics. See Note 15, "Segment, Geographical and Other Revenue Information" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Performance Enzymes

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the pharmaceuticals market, and to date this continues to be our largest market served. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. We have also used the technology to develop customized enzymes for use in other industrial markets. These markets consist of several large industrial verticals, including food and food ingredients, animal feed, flavors, fragrances, and agricultural chemicals. We also use our technology to develop enzymes for customers using NGS and PCR/qPCR for in vitro molecular diagnostic and molecular biology research applications. In April 2018, we entered into the Porton Agreement related to our strategic collaboration with Porton to license key elements of our world-leading biocatalyst technology for use in Porton’s global custom intermediate and API development and manufacturing business.

Novel Biotherapeutics

We are also targeting new opportunities in the pharmaceutical industry to discover, improve, and/or develop biotherapeutic drug candidates. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer’s pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity. Most notable is our lead program for the potential treatment of hyperphenylalaninemia (“HPA”) (also referred to as PKU) in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we announced a strategic collaboration with Nestlé Health Science to advance CDX-6114, our own novel orally administrable enzyme therapeutic candidate for the potential treatment of PKU. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, which was conducted in Australia. In November 2018, we announced top-line results from the Phase 1a study in healthy volunteers with CDX-6114. In December 2018, Nestlé Health Science became obligated to pay us an additional $1.0 million within 60 days after the achievement of a milestone relating to formulation of CDX-6114. In January 2019, we received notice from the U.S. Food and Drug Administration (the “FDA”) that it had completed its review of our investigational new drug application (“IND”) for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive,

worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, Nestlé Health Science is obligated to pay us $3.0 million within 60 days after exercise of the option. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, “Subsequent Events” in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details.

We have also developed a pipeline of other biotherapeutic drug candidates in which we expect to continue to make additional investments with the aim of advancing additional product candidates targeting other therapeutic areas.
For further description of our business segments, see Note 15, "Segment, Geographical and Other Revenue Information," in the Notes to Condensed Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Results of Operations Overview

On January 1, 2018, we adopted Accounting Standards Update, or ASU, 2014-09 “Revenue from Contracts with Customers (Topic 606)” and the related amendments (“ASC 606”). Under the modified retrospective method, we applied the new standard to contracts which were not completed as of January 1, 2018. Results for reporting periods beginning after January 1, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with our historic accounting under ASU 2009-13 “Revenue Recognition”(Topic 605)”. The adoption of ASC 606 limits the comparability of revenue and certain expenses, including revenues and costs and operating expenses, presented in the results of operations for the year ended December 31, 2018 when compared to the years ended December 31, 2017 and 2016. For additional information regarding the adoption of this accounting standard, see Note 2, “Summary of Significant Accounting Policies”, to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Revenues were $60.6 million in 2018, a 21% increase from $50.0 million in 2017. Product revenue, which consists primarily of sales of protein catalysts, pharmaceutical intermediates, and Codex® Biocatalyst Panels and Kits, was $25.6 million in 2018, a decrease of 4% compared with $26.7 million in 2017. The decrease in product revenue is primarily due to variability in our customers’ manufacturing schedules.

Research and development revenues, which include license, technology access and exclusivity fees, research service fees, milestone payments, royalties, and optimization and screening fees, totaled $35.0 million in 2018, an increase of 50%, compared with $23.3 million in 2017. The increase is primarily due to revenues from our collaborative arrangements with Nestlé Health Science for the development of CDX-6114 and development of novel enzymes for Nestlé Health Science under our Strategic Collaboration Agreement, research and development revenue from Tate & Lyle and Merck, and recognition of a license fee and technology transfer from Porton.

Our products’ profitability is affected by many factors including the margin of profit on products we sell. Our profit margins are affected by many factors including the costs of internal and third-party fixed and variable costs, including materials and supplies, labor, facilities and other overhead costs. Profit margin data is used as a management performance measure to provide additional information regarding our results of operations on a consolidated basis.

Product gross margins increased to 51% in 2018, compared to 46% in 2017 due to improved sales mix.

Research and development expenses were $30.0 million in 2018, an increase of 1% from $29.7 million in 2017. The increase was primarily due to an increase in costs associated with higher headcount, higher allocable expenses, increases in lab supplies and stock compensation expense and were partially offset by a decrease in outside services which were mostly related to prior year development costs for project CDX-6114.

Selling, general and administrative expenses were $29.3 million in 2018, an increase of 1% compared to $29.0 million in 2017. The increase was primarily due to increases in costs associated with higher headcount, consulting and outside services, accounting fees, recruiting fees, and stock compensation expenses which were partially offset by a reduction in legal expenses related to 2017 activities and allocable expenses.

Net loss was $10.9 million, or a net loss of $0.21 per share, in 2018 compared to a net loss of $23.0 million, or a net loss of $0.50 per share, in 2017. The decreases in net loss and net loss per share are primarily attributable to a net increase in revenue and reductions in product costs. The net increase in revenue is primarily attributed to research and development revenue from Nestlé Health Science and Tate & Lyle partially offset by a decrease in product revenue. The reduction in product costs reflected the sale of higher gross margin products.

Cash and cash equivalents increased to $53.0 million as of December 31, 2018 compared to $31.2 million as of December 31, 2017. In addition, net cash used in operations was $14.1 million in 2018, as compared to net cash used in operations of $8.8 million in 2017. We believe that based on our current level of operations, our existing cash, cash equivalents, and equity securities will provide adequate funds for ongoing operations, planned capital expenditures and working capital requirements for at least the next 12 months.

In June 2017, we entered into a loan and security agreement that allows us to borrow up to $10.0 million under a term loan, and up to $5.0 million under a revolving credit facility with 80% of certain eligible accounts receivable as a borrowing base (the "Credit Facility"). Obligations under the Credit Facility are secured by a lien on substantially all of our personal property other

than our intellectual property. In September 2018, we entered into a Fourth Amendment to the Credit Facility whereby the draw period on the term debt was extended to September 30, 2019. We may draw on the Term Debt at any time prior to September 30, 2019, subject to customary conditions for funding including, among others, that no event of default exists. As of December 31, 2018, no amounts were borrowed under the Credit Facility and we were in compliance with the covenants for the Credit Facility. See Note 13, "Commitments and Contingencies" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Below is an overview of our results of operations by business segments:

Performance Enzymes

Revenues increased by $4.7 million, or 11%, to $47.1 million in 2018, compared to 2017. The increase in revenues was due primarily to an increase in research and development revenue from Tate & Lyle and Novartis, and the recognition of a license fee and technology transfer from Porton. These increases were partially offset by a decrease in product revenue due to the variability in our customers' manufacturing schedules.

Product gross margins were 51% in 2018, compared to 46% in the corresponding period in 2017. The increase in product gross margins was primarily due an increase in sales of higher margin products combined with a decrease in sales of lower margin products over the prior fiscal period.

Research and development expense increased $2.1 million, or 12%, to $18.9 million in 2018, compared to 2017, due primarily to an increase in costs associated with higher headcount, an increase in lab supplies and stock compensation expenses and an increase related to activities under the Tate and Lyle and Novartis collaboration agreements.

Selling, general and administrative expense increased by $0.2 million, or 2%, to $7.5 million in 2018, compared to the year of 2017, due primarily to an increase in costs associated with higher headcount.

Novel Biotherapeutics

Research and development revenue in 2018 was $13.5 million. Revenues in the Novel Biotherapeutics segment are derived entirely from research and development revenue relating to the development of our CDX-6114 product candidate in collaboration with Nestlé Health Science. In 2017, we signed a global development, option and license agreement with Nestlé Health Science and, thus, we had no revenues in the Novel Biotherapeutics segment prior to 2017.

Research and development expense decreased $1.9 million, or 16%, to $10.2 million in 2018, compared to 2017, due primarily to activities related to the development of our CDX-6114 in the prior year.

Selling, general and administrative expense was $0.8 million in 2018, compared to zero in 2017. This consisted of the allocated employee costs related to the development of our CDX-6114 product candidate and other product candidates in our Novel Biotherapeutics pipeline. De minimis selling, general and administrative expense incurred in 2017 were not allocated to the biotherapeutics segment.

Below is an overview of our collaborative arrangements:

GSK Platform Technology Transfer, Collaboration and License Agreement

In July 2014, we entered into a CodeEvolver® protein engineering platform technology transfer collaboration and license agreement (the "GSK CodeEvolver® Agreement") with GlaxoSmithKline ("GSK"). Pursuant to the terms of the agreement, we granted GSK a non-exclusive license to use the CodeEvolver® protein engineering platform technology to develop novel enzymes for use in the manufacture of GSK's pharmaceutical and health care products. We received an upfront fee upon the execution of the agreement in July 2014 and milestone payments in each of the years from 2014 through April 2016. We completed the transfer of the CodeEvolver® protein engineering platform technology to GSK in April 2016 and all revenues relating to the technology transfer have been recognized as of April 2016. We have the potential to receive additional cumulative contingent payments that range from $5.75 million to $38.5 million per project based on GSK's successful application of the licensed technology. We are also eligible to receive royalties based on net sales of GSK's sales of licensed enzyme products that are currently not being recognized.

Merck Platform Technology Transfer and License Agreement

In August 2015, we entered into a CodeEvolver® platform technology transfer collaboration and license agreement (the "Merck CodeEvolver® Agreement") with Merck, Sharp & Dohme ("Merck") which allows Merck to use the CodeEvolver® protein engineering technology platform in the field of human and animal healthcare.

We received a $5.0 million up-front license fee upon execution of the Merck CodeEvolver® Agreement, and milestone payments in September 2015 and in September 2016, when we completed the transfer of the engineering platform technology. Additionally, we recognized research and development revenues of $4.1 million, $3.6 million, and $3.0 million in 2018, 2017 and 2016, respectively, for various research projects under our collaborative arrangement.

We have the potential to receive payments of up to a maximum of $15.0 million for each commercial API that is manufactured by Merck using one or more novel enzymes developed by Merck using the CodeEvolver® protein engineering technology platform. The API payments, which are currently not recognized as revenue, are based on quantity of API developed and manufactured by Merck and will be recognized as usage-based royalties. In February 2019, we have signed a new agreement with Merck to install certain CodeEvolver® protein engineering technology upgrades into Merck’s platform license installation and will maintain those upgrades for a multi-year term.

In October 2018, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we amended certain licensing provisions and one exhibit. In January 2019, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we will install certain CodeEvolver® protein engineering technology upgrades into Merck’s platform license installation and maintain those upgrades for a multi-year term.

Global Development, Option and License Agreement and Strategic Collaboration Agreement

In October 2017, we entered into the Nestlé Agreement with Nestlé Health Science and, solely for the purpose of the integration and the dispute resolution clauses of the Agreement, Nestlé Health Science S.A., to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU.

We received an upfront cash payment of $14.0 million upon the execution of the Nestlé Agreement and a $4.0 million milestone payment 60 days after dosing the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114 for the potential treatment of PKU. The $4.0 million milestone payment that was triggered by the initiation of the trial was received in September 2018. The upfront payment and the variable consideration relating to the progress payment of $4.0 million are being recognized over time as the development work is being performed. Revenue is being recognized using a single measure of progress that depicts our performance in transferring control of the services, which is based on the ratio of level of effort incurred to date compared to the total estimated level of effort required to complete all performance obligations under the agreement. We recognized development fees of $9.9 million in 2018 as research and development revenue and $7.2 million in 2017. We had deferred revenue under this agreement of $1.9 million at December 31, 2018 and $6.8 million at December 31, 2017.

In December 2018, Nestlé Health Science became obligated to pay us an additional $1.0 million within 60 days after the achievement of a milestone relating to formulation of CDX-6114. In January 2019, we received notice from the U.S. Food and Drug Administration (the “FDA”) that it had completed its review of our investigational new drug application (“IND”) for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, Nestlé Health Science is obligated to pay us $3.0 million within 60 days after exercise of the option. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, “Subsequent Events” in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details.

We are also eligible to receive payments from Nestlé Health Science under the Nestlé Agreement that include (i) development and approval milestones of up to $86.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of Product.

In addition to the Nestlé Agreement, we and Nestlé Health Science concurrently entered into a Strategic Collaboration Agreement (the "Strategic Collaboration Agreement") pursuant to which we and Nestlé Health Science will collaborate to leverage the CodeEvolver® protein engineering technology platform to develop novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. Under the Strategic Collaboration Agreement, we received an

upfront payment of $1.2 million in 2017 and an incremental $0.6 million payment in September 2018 for additional services. We recognized research and development fees of $3.6 million and $0.5 million in 2018 and 2017, respectively. As of December 31, 2018 and 2017, we had deferred revenue of $0.8 million and $1.1 million, respectively.

Strategic Collaboration Agreement

In April 2018, we entered into the Porton Agreement with Porton to license key elements of Codexis' biocatalyst technology for use in Porton's global custom intermediate and API development and manufacturing business. Under the Porton Agreement, we are eligible to receive annual collaboration fees and research and development revenues. We received an initial collaboration fee of $0.5 million within 30 days of the effective date of the agreement. As of December 31, 2018, we completed the technical transfer and we recognized revenue of $2.8 million in 2018 as research and development revenue. Revenue relating to the functional license provided to Porton was recognized at a point in time when control of the license transferred and technology transfer to the customer. We have the potential to receive performance payments based on products produced by Porton using our company's technology under the license agreement.

Recent Accounting Pronouncements

For information on recent accounting pronouncements, see Note 2, "Summary of Significant Accounting Policies", to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Financial results for the year ended December 31, 2018, as compared to the year ended December 31, 2017, reflect the effects of adopting ASU 2014-09, "Revenue from Contracts with Customers (Topic 606)," and the related amendments ("ASC 606"), which provided a new basis of accounting for our revenue arrangements during fiscal 2018.

The adoption of ASC 606 limits the comparability of revenue and certain expenses, including revenues and costs and operating expenses, presented in the results of operations for the year ended December 31, 2018 when compared to the year ended December 31, 2017. For additional information regarding the impact from adoption of this accounting standard, see Note 3, "Revenue Recognition" to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Results of Operations

The following table shows the amounts from our consolidated statements of operations for the periods presented (in thousands, except percentages):

	Year Ended December 31,			% of Total Revenues		
	2018	2017	2016	2018	2017	2016
Revenues:						
Product revenue	$25,590	$26,685	$15,321	42 %	53 %	31 %
Research and development revenue	35,004	23,339	33,516	58 %	47 %	69 %
Total revenues	60,594	50,024	48,837	100 %	100 %	100 %
Costs and operating expenses:						
Cost of product revenue	12,620	14,327	9,753	21 %	29 %	20 %
Research and development	29,978	29,659	22,229	50 %	59 %	46 %
Selling, general and administrative	29,291	29,008	25,419	48 %	58 %	52 %
Total costs and operating expenses	71,889	72,994	57,401	119 %	146 %	118 %
Loss from operations	(11,295)	(22,970)	(8,564)	(19)%	(46)%	(18)%
Interest income	671	147	60	1 %	— %	— %
Other expense, net	(291)	(92)	(94)	— %	— %	— %
Loss before income taxes	(10,915)	(22,915)	(8,598)	(18)%	(46)%	(18)%
Provision for (benefit from) income taxes	(37)	81	(40)	— %	— %	— %
Net loss	$(10,878)	$(22,996)	$(8,558)	(18)%	(46)%	(18)%

Revenues

Our revenues are comprised of product revenue and research and development revenue as follows:

- Product revenue consist of sales of protein catalysts, pharmaceutical intermediates, and Codex® Biocatalyst Panels and Kits.
- Research and development revenue include license, technology access and exclusivity fees, research services fees, milestone payments, royalties, optimization and screening fees, and revenue sharing arrangement based upon sales of licensed products by our former revenue sharing partner, Exela PharmSci, Inc. ("Exela") in 2017 and 2016.

Revenues is as follows (in thousands, except percentages):

				Change			
	Year Ended December 31,			2018		2017	
	2018	2017	2016	$	%	$	%
Product revenue	$25,590	$26,685	$15,321	$(1,095)	(4)%	$11,364	74%
Research and development revenue	35,004	23,339	33,516	11,665	50%	(10,177)	(30)%
Total revenues	$60,594	$50,024	$48,837	$10,570	21%	$1,187	2%

Revenues typically fluctuate on a quarterly basis due to the variability in our customers' manufacturing schedules and the timing of our customers' clinical trials. In addition, we have limited internal capacity to manufacture enzymes. As a result, we are dependent upon the performance and capacity of third party manufacturers for the commercial scale manufacturing of the enzymes used in our pharmaceutical and fine chemicals business.

We accept purchase orders for deliveries covering periods from one day up to approximately one year from the date on which the order is placed. However, a majority of the purchase orders can be revised or cancelled by the customer without penalty. Considering these industry practices and our experience, we do not believe the total of customer purchase orders outstanding (backlog) provides meaningful information that can be relied on to predict actual sales for future periods.

2018 compared to 2017

Total revenues increased by $10.6 million in 2018 to $60.6 million, as compared to 2017. The increase was driven by growth in research and development revenue of $11.7 million or 50%, partially offset by a decrease of $1.1 million in product revenue.

Product revenue, which consist primarily of sales of protein catalysts, pharmaceutical intermediates, and Codex® Biocatalyst Panels and Kits, were $25.6 million in 2018, a decrease of 4% compared with $26.7 million in 2017. The decrease was primarily due to variability in our customers' manufacturing schedules.

Research and development revenue increased by $11.7 million in 2018 to $35.0 million, as compared to 2017, primarily due to revenues from our arrangements with Nestlé Health Science for the development of CDX-6114 and development of novel enzymes for Nestlé Health Science under our Strategic Collaboration Agreement, research and development revenue from Tate & Lyle, Merck and Novartis, and on the recognition of a functional license fee and technology transfer from Porton.

2017 compared to 2016

Total revenues increased by $1.2 million in 2017 to $50.0 million, as compared to 2016. The increase was driven by an increase in product revenue of $11.4 million or 74%, offset by a decrease of $10.2 million in research and development revenue.

Product revenue, which consist primarily of sales of protein catalysts, pharmaceutical intermediates, and Codex® Biocatalyst Panels and Kits, were $26.7 million in 2017, an increase of 74% compared with $15.3 million in 2016. The increase was primarily due to higher customer demand in 2017 as compared to 2016, in particular higher sales of enzymes to the existing 2016 customer base.

Research and development revenue decreased by $10.2 million in 2017 to $23.3 million, as compared to 2016. The revenue decrease in 2017 was primarily due to the absence of $22.5 million of non-recurring revenues from the technology transfer of our proprietary CodeEvolver® protein engineering platform technology to Merck and GSK in 2016, which was comprised of a milestone payment of $8.0 million from Merck, a milestone payment of $7.5 million from GSK and $7.0 million in recognition of license fees under both agreements. The revenue decrease in 2017 was partially offset by revenues of $13.1 million for research services under our agreements with Nestlé Health Sciences,

Tate & Lyle, Novartis, and revenue sharing arrangement revenues from Exela.

Cost and Operating Expenses (in thousands, except percentages):

	Year Ended December 31,			Change 2018		2017	
	2018	2017	2016	$	%	$	%
Cost of product revenue	$12,620	$14,327	$9,753	$(1,707)	(12)%	$4,574	47%
Research and development	29,978	29,659	22,229	319	1%	7,430	33%
Selling, general and administrative	29,291	29,008	25,419	283	1%	3,589	14%
Total costs and operating expenses	$71,889	$72,994	$57,401	$(1,105)	(2)%	$15,593	27%

Cost of Product Revenue and Product Gross Margin

Our revenues from product revenue are derived entirely from our Performance Enzymes segment. Revenues from the Novel Biotherapeutics segment are from collaborative research and development activities and not from product revenue.

The following table shows the amounts of our product revenue, cost of product revenue, product gross profit and product gross margin from our consolidated statements of operations for the years ended (in thousands, except percentages):

	Year Ended December 31,		Change		Year Ended December 31,		Change	
	2018	2017	$	%	2017	2016	$	%
Product revenue	$25,590	$26,685	$(1,095)	(4)%	$26,685	$15,321	$11,364	74%
Cost of product revenue [1]	12,620	14,327	(1,707)	(12)%	14,327	9,753	4,574	47%
Product gross profit	$12,970	$12,358	$612	5%	$12,358	$5,568	$6,790	122%
Product gross margin (%) [2]	51%	46%			46%	36%		

[1] Cost of product revenue comprises both internal and third-party fixed and variable costs, including materials and supplies, labor, facilities and other overhead costs associated with our product revenue.

[2] Product gross margin is used as a performance measure to provide additional information regarding our results of operations on a consolidated basis.

2018 compared to 2017

Cost of product revenue decreased by $1.7 million in 2018 to $12.6 million, as compared to 2017. The decrease was primarily due to a reduction in costs associated with a reduction in product revenue. Product gross margin increased to 51% in 2018 as compared to 46% in 2017 due to the change in sales mix as we had an increase in sales of higher margin products in 2018 compared to 2017.

2017 compared to 2016

Cost of product revenue increased by $4.6 million in 2017 to $14.3 million, as compared to 2016. The increase was primarily due to higher product revenue from increased customer demand. Product gross margin increased to 46% in 2017 as compared to 36% in 2016 due to improved sales mix.

Research and Development Expenses

Research and development expenses consist of costs incurred for internal projects as well as collaborative research and development activities. These costs primarily consist of (i) employee-related costs, which include salaries and other personnel-related expenses (including stock-based compensation), (ii) various allocable expenses, which include occupancy-related costs, supplies, depreciation of facilities and laboratory equipment, and (iii) external costs. Research and development expenses are expensed when incurred.

2018 compared to 2017

Research and development expenses were $30.0 million in 2018 compared to $29.7 million in 2017, an increase of $0.3 million or 1%. The increase was primarily due to $1.9 million in costs associated with higher headcount, $1.1 million in higher allocable expenses which include occupancy-related costs and supplies, and increases of $0.7 million in lab supplies, $0.6 million in stock compensation expenses, and $1.0 million increase in repairs and maintenance costs, outside consultants and travel costs. These increases were partially offset by a decrease of $4.9 million in outside services which were mostly related to prior year development costs for project CDX-6114.

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2017 compared to 2016

Research and development expenses were $29.7 million in 2017 compared to $22.2 million in 2016, an increase of $7.4 million or 33%. The increase was primarily due to a $7.2 million increase in outside services, which were mostly related to the development project for CDX-6114, an increase of $1.5 million in costs associated with higher headcount relating to additional research and development projects, including the development of CDX-6114, and an increase of $0.7 million in lab supplies, which were partially offset by lower amortization of intangibles.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist of employee-related costs, which include salaries and other personnel-related expenses (including stock-based compensation), hiring and training costs, consulting and outside services expenses (including audit and legal counsel related costs), marketing costs, building lease costs, and depreciation expenses.

2018 compared to 2017

Selling, general and administrative expenses were $29.3 million in 2018 compared to $29.0 million in 2017, an increase of $0.3 million or 1%. The increase was primarily due to increases of $1.2 million in salaries and personnel costs associated with higher headcount, $1.0 million in consulting and outside services, $0.4 million in recruiting fees, $0.3 million in accounting fees and $0.2 million in stock compensation expense which were partially offset by a decrease of $1.1 million in allocable expenses and $1.8 million in legal expenses related to 2017 activities.

2017 compared to 2016

Selling, general and administrative expenses were $29.0 million in 2017 compared to $25.4 million in 2016, an increase of $3.6 million or 14%. The increase was primarily due to an increase of $1.9 million in costs associated with higher headcount, including stock-based compensation costs, an increase of $1.2 million in legal expenses relating to intellectual property and higher consulting fees, partially offset by lower depreciation expense.

Other Income (Expense), net (in thousands, except percentages):

	Year Ended December 31,			Change 2018		Change 2017	
	2018	2017	2016	$	%	$	%
Interest income	$671	$147	$60	$524	356%	$87	145%
Other expense, net	(291)	(92)	(94)	199	216%	(2)	(2)%
Total other income (expense), net	$380	$55	$(34)	$325	591%	$89	262%

Interest Income

Interest income increased by $0.5 million in 2018 compared to 2017, and increased by $87 thousand in 2017 compared to 2016. The changes were primarily due to higher interest rates on higher levels of cash, cash equivalents and short-term investment portfolio balances.

Other Expense

Other expense increased by $0.2 million in 2018 compared to 2017 primarily due to an unrealized loss of $83 thousand related to our investment in CO2 Solutions and expenses due to fluctuations in foreign currency. Other expense decreased by $2 thousand in 2017 compared to 2016, primarily due to fluctuations in foreign currency.

Provision for (benefit from) Income Taxes (in thousands, except percentages):

	Year Ended December 31,			Change 2018		Change 2017	
	2018	2017	2016	$	%	$	%
Provision for (benefit from) income taxes	$ (37)	$ 81	$ (40)	$118	146%	$(121)	(303)%

The benefit from income taxes for 2018 is primarily related to a net loss from our foreign operations and a reduction in the deferred tax liability for accrued future withholding taxes on dividends. The provision for income taxes in 2017 is primarily

related to taxes on foreign earnings and an increase in the deferred tax liability for accrued future withholding taxes on dividends. The benefit from income taxes for 2016 is primarily related to a reduction in the deferred tax liability for accrued future withholding taxes on dividends. We continue to maintain a full valuation allowance against our net deferred tax assets as we believe that it is more likely than not that the majority of our deferred tax assets will not be realized.

Net Loss

Net loss for 2018 was $10.9 million, or a net loss per basic and diluted share of $0.21. This compares to a net loss of $23.0 million, or a net loss per basic and diluted share of $0.50 for 2017. The decreases in net loss is primarily attributable a net increase in revenue and reductions in product costs. The net increase in revenue is primarily attributed to research and development revenue from Nestlé Health Science and Tate & Lyle partially offset by a decrease in product revenue due to variability in our customers' manufacturing schedules. The reduction in product costs reflected the sale of higher gross margins products partially offset by lower costs associated with the reduction in product revenue.

The increase in net loss for 2017 over a net loss of $8.6 million, or a net loss per basic and diluted share of $0.21, for 2016 is primarily related to a decrease in research and development revenues and an increase in research and development expenses which were partially offset by an increase in product revenue.

Results of Operations by Segment (in thousands, except percentages)

Revenues by segment

	Year Ended December 31, 2018			Year Ended December 31, 2017			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Revenues:										
Product revenue	$25,590	$ —	$25,590	$26,685	$ —	$26,685	$(1,095)	(4)%	$ —	—%
Research and development revenue	21,483	13,521	35,004	15,648	7,691	23,339	5,835	37%	5,830	76%
Total revenues	$47,073	$ 13,521	$60,594	$42,333	$ 7,691	$50,024	$4,740	11%	$ 5,830	76%

Revenues from the Performance Enzymes segment increased by $4.7 million, or 11%, to $47.1 million in 2018, compared to $42.3 million in 2017 primarily due to an increase in research and development revenue from Tate & Lyle, Merck and Novartis, and on the recognition of a functional license fee from Porton. This increase was partially offset by a decrease in product revenue primarily due to variability in our customers' manufacturing schedules.

Revenues from the Novel Biotherapeutics segment increased by $5.8 million, or 76%, to $13.5 million in 2018, compared to $7.7 million in 2017. Revenues from the Novel Biotherapeutics segment are derived primarily from research and development revenue relating to the development of our CDX-6114 product candidate in collaboration with Nestlé Health Science. Our dependence on revenues generated from Nestlé Health Science, if lost, would have a material adverse effect on the Novel Biotherapeutics segment.

Costs and operating expenses by segment

	Year Ended December 31, 2018			Year Ended December 31, 2017			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Cost of product revenue	$12,620	$ —	$12,620	$14,327	$ —	$14,327	$(1,707)	(12)%	$—	—%
Research and development[1]	18,924	10,185	29,109	16,847	12,107	28,954	2,077	12%	(1,922)	(16)%
Selling, general and administrative[1]	7,538	771	8,309	7,371	—	7,371	167	2%	771	100%
Total segment costs and operating expenses	$39,082	$ 10,956	50,038	$38,545	$ 12,107	50,652	$537	1%	$(1,151)	(10)%
Corporate costs			20,704			21,300				
Depreciation			1,147			1,042				
Total costs and operating expenses			$71,889			$72,994				

[1] Research and development expenses and Selling, general and administrative expenses exclude depreciation.

For a discussion of product cost of revenue, see “Results of Operations”.

Research and development expense in the Performance Enzymes segment increased by $2.1 million, or 12%, to $18.9 million in 2018, compared to $16.8 million in 2017. The increase was primarily due to $2.2 million in associated with increased headcount, $0.6 million in lab supplies costs and $0.5 million in stock compensation expenses. These increases were partially offset by a decrease of $1.2 million in allocable expenses, which include occupancy-related costs, supplies, and depreciation expense.

Selling, general and administrative expense in the Performance Enzymes segment increased by $0.2 million, or 2%, to $7.5 million in 2018, compared to $7.4 million in 2017. The increase was primarily due to $0.8 million in higher costs associated with increased headcount, partially offset by a decrease of $0.4 million in lower allocable expenses and $0.2 million in lower stock compensation expense.

Research and development expense in the Novel Biotherapeutics segment decreased by $1.9 million, or 16%, to $10.2 million in 2018, compared to $12.1 million in 2017. The decrease was primarily due to $4.9 million in lower costs associated with a reduction in the outside research and development services used in the development of the CDX-6114 product candidate. The decrease was partially offset by a $2.3 million increase in allocable expenses, a $0.6 million increase in costs associated with higher headcount and a $0.1 million increase in stock compensation expense.

Selling, general and administrative expense in the Novel Biotherapeutics segment was $0.8 million in 2018 and primarily consisted of $0.5 million in allocable costs and $0.2 million in costs associated with headcount. Selling, general and administrative expense in the Novel Biotherapeutics segment was zero in 2017. De minimis selling, general and administrative expense incurred in 2017 were not allocated to the biotherapeutics segment.

Income (loss) from operations by segment

	Year Ended December 31, 2018			Year Ended December 31, 2017			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Income (loss) from operations	$7,991	$ 2,565	10,556	$3,788	$ (4,416)	(628)	$4,203	111%	$6,981	158%

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Income from operations in the Performance Enzymes segment increased $4.2 million, or 111%, to $8.0 million, in 2018, compared to $3.8 million in 2017. The increase in income from operations was primarily due to an increase in research and development revenue, a reduction in product costs associated with a decline in product revenue and a reduction in product costs associated with the sale of higher margin products. These were partially offset by a decrease in product revenues and an increase in research and development costs.

Income from operations in the Novel Biotherapeutics segment increased $7.0 million, or 158%, to $2.6 million in 2018 compared to in 2017. The increase in income from operation was primarily due to $5.8 million in revenue from the development of our CDX-6114 product candidate in collaboration with Nestlé Health Science, partially offset by lower costs associated with a reduction in the outside research and development services used in the CDX-6114 product candidate development.

Previously, we had only one business segment. As our biotherapeutics business has emerged as a significant opportunity for us, effective in 2018, we formed Novel Biotherapeutics as a new business segment. The Novel Biotherapeutics segment focuses on new opportunities in the pharmaceutical industry to discover or improve novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. The Performance Enzymes segment consists of the existing protein catalyst products and services with focus on pharmaceutical, food, molecular diagnostics, and other industrial markets. See Note 15, "Segment, Geographical and Other Revenue Information" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for information about revenues by geographic area, long-lived assets by geographic area, and revenues by major customers.

Liquidity and Capital Resources

Liquidity is the measurement of our ability to meet working capital needs and to fund capital expenditures. We have historically funded our operations primarily through cash generated from operations, stock option exercises and public offerings of our common stock. We also have the ability to borrow up to $15.0 million under our Credit Facility. We actively manage our cash usage and investment of liquid cash to ensure the maintenance of sufficient funds to meet our working capital needs. The majority of our cash and cash equivalents are held in U.S. banks, and our foreign subsidiaries maintain a limited amount of cash in their local banks to cover their short-term operating expenses.

The following summarizes our cash and cash equivalents balance and working capital as of December 31, 2018, 2017 and 2016:

	December 31,		
(In Thousands)	2018	2017	2016
Cash and cash equivalents	$53,039	$31,219	$19,240
Working capital	50,085	20,087	14,860

In addition to our existing cash and cash equivalents, we are eligible to earn milestone and other contingent payments for the achievement of defined collaboration objectives and certain royalty payments under our collaboration agreements. Our ability to earn these milestone and contingent payments and the timing of achieving these milestones is primarily dependent upon the outcome of our collaborators' research and development activities and is uncertain at this time. In the third quarter of 2016, we completed the final phase in the transfer of CodeEvolver® technology to Merck under the Merck CodeEvolver® Agreement. Following the completion of the technology transfer to Merck, we are now eligible to receive payments of up to $15.0 million for each commercial API that is manufactured by Merck using one or more novel enzymes developed by Merck using the CodeEvolver® technology. In addition, depending upon GSK's successful application of the licensed technology, we have the potential to receive additional contingent payments that range from $5.75 million to $38.5 million per project.

We are actively collaborating with new and existing customers in the pharmaceutical and food industries. We believe that we can utilize our current products and services, and develop new products and services, to increase our revenues and gross margins in future periods.

We have historically experienced negative cash flows from operations as we continue to invest in key technology development projects and improvements to our CodeEvolver® protein engineering technology platform, and expand

our business development and collaboration with new customers. Our cash flows from operations will continue to be affected principally by sales and gross margins from licensing our technology to major pharmaceutical companies, product sales and collaborative

research and development services provided to customers, as well as our headcount costs, primarily in research and development. Our primary source of cash flows from operating activities is cash receipts from licensing our technology to major pharmaceutical companies, and our customers for purchases of products and/or collaborative research and development services. Our largest uses of cash from operating activities are for employee-related expenditures, rent payments, inventory purchases to support our product sales and non-payroll research and development costs.

On December 9, 2016, we filed a registration statement on Form S-3 with the SEC, under which we may sell an aggregate of up to $80.0 million of common stock, preferred stock, debt securities, warrants, purchase contract and/or units. The SEC declared the registration statement effective on January 10, 2017. Subsequently, in April 2017, we completed an underwritten public offering of approximately 6.3 million shares of our common stock at an offering price of $4.00 per share. The net proceeds to us were approximately $23.8 million after deducting offering costs and the underwriting discounts and commissions. In April 2018, we completed an underwritten public offering of 4.3 million shares of our common stock at a public offering price of $9.25 per share resulting in net proceeds of approximately $37.3 million after deducting the underwriting discounts and commissions.

In June 2017, we entered into the Credit Facility, which consists of term debt for loans that allow us to borrow up to $10.0 million and a revolving credit facility that allows us to borrow up to $5.0 million with a certain eligible accounts receivable borrowing base of 80% of eligible accounts receivable. In September 2018, we entered into a Fourth Amendment to the Credit Facility whereby the draw period on the term debt was extended to September 30, 2019. We may draw on the term debt at any time prior to September 30, 2019, subject to customary conditions for funding including, among others, that no event of default exists. Draws on the Credit Facility are secured by a lien on substantially all of our personal property other than our intellectual property. We may draw on the revolving line of credit at any time prior to the maturity date. On October 1, 2022, any loans for Term Debt mature and the Revolving Line of Credit terminates. No amounts were drawn down under the credit facility as of December 31, 2018. At December 31, 2018, we were in compliance with the covenants for the Credit Facility. The Credit Facility requires us to maintain compliance with certain financial covenants including attainment of certain lender-approved projections or maintenance of certain minimum cash levels. Restrictive covenants in the Credit Facility restrict the payment of dividends or other distributions. For additional information about our contractual obligations, see Note 13 "Commitments and Contingencies" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

In October 2017, we entered into the Nestlé Agreement with Nestlé Health Science. Pursuant to the Nestlé Agreement, Nestlé Health Science paid us an upfront cash payment of $14.0 million. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114 for the potential treatment of PKU. The initiation of the trial triggered a $4.0 million milestone payment from Nestlé Health Science which was paid in September 2018. In December 2018, Nestlé Health Science became obligated to pay us an additional $1.0 million within 60 days after the achievement of a milestone relating to formulation of CDX-6114. In January 2019, we received notice from the U.S. Food and Drug Administration (the “FDA”) that it had completed its review of our investigational new drug application (“IND”) for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, Nestlé Health Science is obligated to pay us $3.0 million within 60 days after exercise of the option. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, “Subsequent Events” in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details. Other potential payments from Nestlé Health Science to us under the Nestlé Agreement include (i) development and approval milestones of up to $86.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of Product.

As of December 31, 2018, we had cash and cash equivalents of $53.0 million and $15.0 million available to borrow under our Credit Facility. Our liquidity is dependent upon our cash and cash equivalents, cash flows provided by operating activities and the continued availability of borrowings under our Credit Facility. We may need additional capital if our current plans and assumptions change. Our need for additional capital will depend on many factors, including the financial success of our business, the spending required to develop and commercialize new and existing products, the effect of any acquisitions of other businesses, technologies or facilities that we may make or develop in the future, our spending on new market opportunities, and the potential costs for the filing, prosecution, enforcement and defense of patent claims, if necessary.

We believe that, based on our current level of operations, our existing cash and cash equivalents will provide adequate funds for ongoing operations, planned capital expenditures and working capital requirements for at least the next 12 months.

However, we may need additional capital if our current plans and assumptions change. Our need for additional capital will depend on many factors, including the financial success of our business, the spending required to develop and commercialize new and existing products, the effect of any acquisitions of other businesses, technologies or facilities that we may make or develop in the future, our spending on new market opportunities, and the potential costs for the filing, prosecution, enforcement and defense of patent claims, if necessary. If our capital resources are insufficient to meet our capital requirements, and we are unable to enter into or maintain collaborations with partners that are able or willing to fund our development efforts or commercialize any products that we develop or enable, we will have to raise additional funds to continue the development of our technology and products and complete the commercialization of products, if any, resulting from our technologies. If future financings involve the issuance of equity securities, our existing stockholders would suffer dilution. If we raise debt financing or enter into credit facilities, we may be subject to restrictive covenants that limit our ability to conduct our business. We may not be able to raise sufficient additional funds on terms that are favorable to us, if at all. If we fail to raise sufficient funds and fail to generate sufficient revenues to achieve planned gross margins and to control operating costs, our ability to fund our operations, take advantage of strategic opportunities, develop products or technologies, or otherwise respond to competitive pressures could be significantly limited. If this happens, we may be forced to delay or terminate research or development programs or the commercialization of products resulting from our technologies, curtail or cease operations or obtain funds through collaborative and licensing arrangements that may require us to relinquish commercial rights, or grant licenses on terms that are not favorable to us. If adequate funds are not available, we will not be able to successfully execute our business plan or continue our business.

Cash Flows

The following is a summary of cash flows for the years ended December 31, 2018, 2017 and 2016:

	Year Ended December 31,		
(In Thousands)	2018	2017	2016
Net cash used in operating activities	$(14,094)	$(8,755)	$(1,860)
Net cash used in investing activities	(2,766)	(983)	(846)
Net cash provided by (used in) financing activities	38,569	21,650	(490)
Net increase (decrease) in cash, cash equivalents and restricted cash	$21,709	$11,912	$(3,196)

Cash Flows from Operating Activities

Cash used in operating activities was $14.1 million in 2018, which resulted from a net loss of $10.9 million adjusted for non-cash depreciation of $1.1 million and stock-based compensation of $7.9 million, as well as changes in operating assets and liabilities. The net change in operating assets and liabilities included decreases in deferred revenue of $10.6 million primarily related to the Nestlé Agreement, and a combined increase in accounts receivable and unbilled receivables of $1.4 million.

Cash used in operating activities was $8.8 million in 2017, which resulted from a net loss of $23.0 million adjusted for non-cash depreciation of $1.0 million and stock-based compensation of $7.1 million, as well as changes in operating assets and liabilities. The net change in operating assets and liabilities included increases in deferred revenue of $11.0 million primarily related to the Nestlé Agreement, an increase in accounts receivable and unbilled accounts receivables of $5.7 million, and an increase in other accrued liabilities of $1.4 million, offset by lower accounts payable of $0.8 million due to the timing of payment of invoices.

Cash used in operating activities was $1.9 million in 2016, which resulted from a net loss of $8.6 million adjusted for non-cash depreciation and amortization of $4.5 million and stock-based compensation of $5.7 million, as well as changes in operating assets and liabilities. The net change in operating assets and liabilities included decreases in deferred revenue of $6.4 million primarily related to revenue recognition on the achievement of milestones from collaborative arrangements with Merck and GSK, partially offset by a decrease in accounts receivable of $1.4 million, and increases in accrued compensation of $1.0 million primarily due to higher payroll costs and higher accounts payable of $0.9 million due to the timing of payment of invoices.

Cash Flows from Investing Activities

Cash used in investing activities was $2.8 million in 2018 primarily due to the purchase of property and equipment. We expect our capital spending including replacement and upgrades of lab equipment and information technology

equipment will be higher in 2019 as compared to 2018.

Cash used in investing activities was $1.0 million in 2017, primarily due to the purchase of property and equipment.

Cash used investing activities was $0.8 million in 2016, primarily due to the purchase of property and equipment.

Cash Flows from Financing Activities

Cash provided by financing activities was $38.6 million in 2018, primarily due to net proceeds from our offering of common stock after deducting underwriting discounts and commission and related costs and proceeds from the exercises of employee stock options which were partially offset by the payment of taxes related to the net share settlement of equity awards.

Cash provided by financing activities was $21.7 million in 2017, primarily due to net proceeds from our offering of common stock after deducting underwriting discounts and commission and related costs and proceeds from the exercises of employee stock options which were partially offset by the payment of taxes related to the net share settlement of equity awards.

Cash used in financing activities was $0.5 million in 2016, which was the result of the payment of taxes related to the net share settlement of equity awards, partially offset by the proceeds from the exercises of employee stock options.

Contractual Obligations

The following table summarizes our significant contractual obligations at December 31, 2018 (in thousands):

	Payments due by period				
	Total	Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years
Capital lease obligations	$313	$252	$61	$ —	$ —
Operating leases obligations [1]	4,523	3,280	1,202	41	—
Total [2]	$4,836	$3,532	$1,263	$ 41	$ —

(1) Represents future minimum lease payments under non-cancellable operating leases in effect as of December 31, 2018 for our facilities in Redwood City, California. The minimum lease payments above do not include common area maintenance charges or real estate taxes. Minimum payments have not been reduced by future minimum sublease rentals of $0.9 million to be received under non-cancellable subleases.

(2) Excludes $0.7 million of uncertain tax liabilities for which we cannot make a reasonably reliable estimate of the period of cash settlement.

In February 2019, we entered into the eighth lease amendment ("Eighth Amendment") with MetLife for our buildings to extend the lease term to another 88 months except for building 101. The various terms for the remaining spaces under the Eighth Amendment have expiration dates that range from May 2027 to May 2029. See Note 16, “Subsequent Events” in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for additional information. Future minimum lease payments under the Eighth Amendment are as follows (in thousands):

	Payments due by period				
	Total	Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years
Operating leases obligations	$32,865	$ —	$5,812	$8,833	$18,220

Other Commitments

We have other commitments related to supply and service arrangements entered into in the normal course of business. For additional information about other commitments, see Note 13 "Commitments and Contingencies" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K. Future minimum payments reflect amounts those obligations are expected to have on our liquidity and cash flows in future period and include obligations subject to risk of cancellation by us (in thousands):

Other Commitment Agreement Type	Agreement Date	Future Minimum Payment
Manufacture and supply agreement with expected future payment date of December, 2022	April 2016	$ 1,458
Service agreement for stability study	July 2017	331
Service agreement for clinical trial	December 2017	1,258
Total other commitments		$ 3,047

Credit Facility

In June 2017, we entered into a credit facility (“Credit Facility”) consisting of term loans (“Term Debt”) up to $10.0 million, and advances (“Advances”) under a revolving line of credit (“Revolving Line of Credit”) up to $5.0 million with an accounts receivable borrowing base of 80% of eligible accounts receivable. At December 31, 2018, we have not drawn from the Credit Facility. We may draw on the Revolving Line of Credit at any time prior to the September 30, 2019 maturity date. On October 1, 2022, loans drawn under the Term Debt mature and the Revolving Line of Credit terminates. Loans made under the Term Debt bear interest through maturity at a variable rate based upon the LIBOR rate plus 3.6%. Advances made under the Revolving Line of Credit bear interest at a variable annual rate equal to the greater of (i) 1.00% above the prime rate and (ii) 5.00%.

Our obligations under the Credit Facility are secured by a lien on substantially all of our personal property other than our intellectual property. The Credit Facility includes a number of customary covenants and restrictive financial covenants including meeting minimum product revenues levels and maintaining certain minimum cash levels with the lender. The Credit Facility’s financial covenants restrict the ability of the Company to transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay dividends or make other distributions, make investments, create liens, sell assets, or sell certain assets held at foreign subsidiaries. A failure to comply with these covenants could permit the lender to exercise remedies against us and the collateral securing the Credit Facility, including foreclosure of our properties securing the Credit Facilities and our cash. At December 31, 2018, we were in compliance with the covenants for the Credit Facility.

For additional information about our credit facility, see Note 13 "Commitments and Contingencies" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Off-Balance Sheet Arrangements

As of December 31, 2018, we had no off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the SEC.

Critical Accounting Policies and Estimates

Management’s discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements. The consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States and include our accounts and the accounts of our wholly-owned subsidiaries. The preparation of our consolidated financial statements requires our management to make estimates, assumptions, and judgments that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the applicable periods. Management bases its estimates, assumptions and judgments on historical experience and on various other factors that are believed to be reasonable under the circumstances. Different assumptions and judgments would change the estimates used in the preparation of our consolidated financial statements, which, in turn, could change the results from those reported. Our management evaluates its estimates, assumptions and judgments on an ongoing basis.

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The critical accounting policies requiring estimates, assumptions, and judgments that we believe have the most significant impact on our consolidated financial statements are described below.

Revenue Recognition

Policy from January 1, 2018

On January 1, 2018, we adopted the provisions of ASU 2014-09, "Revenue from Contracts with Customers (Topic 606)" and the related amendments ("ASC 606"). The guidance provides a unified model to determine how revenue is recognized.

Our revenues are derived primarily from product revenue and collaborative research and development agreements. The majority of our contracts with customers typically contain multiple products and services. We account for individual products and services separately if they are distinct-that is, if a product or service is separately identifiable from other items in the contract and if a customer can benefit from it on its own or with other resources that are readily available to the customer.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our product revenue and collaborative research and development agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

The majority of our collaborative contracts contain multiple revenue streams such as up-front and/or annual license fees, fees for full time employee ("FTE") research and development services, contingent milestone payments upon achievement of contractual criteria, and royalty fees based on the licensees' product revenue or usage, among others. We determine the stand-alone selling price ("SSP") and allocate consideration to distinct performance obligations. Typically, we base our SSPs on our historical sales. If an SSP is not directly observable, then we estimate the SSP taking into consideration market conditions, forecasted sales, entity-specific factors and available information about the customer. We estimate the SSP for license rights by using a discounted cash flow method which includes the following key assumptions: the development timelines, revenue forecasts, commercialization expenses, discount rate, and the probability of technical and regulatory success. For licenses that have been previously sold to other customers, we use historical information to determine SSP.

We account for a contract with a customer when there is approval and commitment from both parties, the rights of the parties are identified, payment terms are identified, the contract has commercial substance and collectability of consideration is probable. Non-cancellable purchase orders received from customers to deliver a specific quantity of product, when combined with our order confirmation, in exchange for future consideration, create enforceable rights and obligations on both parties and constitute a contract with a customer.

We measure revenue based on the consideration specified in the contract with each customer, net of any sales incentives and taxes collected on behalf of government authorities. We recognize revenue in a manner that best depicts the transfer of promised goods or services to the customer, when control of the product or service is transferred to a customer. We make significant judgments when determining the appropriate timing of revenue recognition.

The following is a description of principal activities from which we generate revenue:

Product Revenue

Product revenue consist of sales of protein catalysts, pharmaceutical intermediates and Codex® Biocatalyst Panels and Kits. A majority of our product revenue is made pursuant to purchase orders or supply agreements and is recognized at a point in time when the control of the product has been transferred to the customer typically upon shipment. For some of the products that we develop, we recognize revenue over time as the product is manufactured because we have a right to payment from the customer under a binding, non-cancellable purchase order, and there is no alternate use of the product for us as it is specifically made for the customer's use.

Certain of our agreements provide options to customers which they can exercise at a future date, such as the option to purchase our product during the contract duration at discounted prices and an option to extend their contract, among others. In accounting for customer options, we determine whether an option is a material right and this requires us to

exercise significant judgment. If a contract provides the customer an option to acquire additional goods or services at a discount that exceeds the range of discounts that we typically give for that product or service, or if the option provides the customer certain additional goods or services for free, the option may be considered a material right. If the contract gives the customer the option to acquire

additional goods or services at their normal SSPs, we would likely determine that the option is not a material right and, therefore, account for it as a separate performance obligation when the customer exercises the option. We primarily account for options which provide material rights using the alternative approach available under ASC 606, as we concluded we meet the criteria for using the alternative approach. Therefore, the transaction price is calculated as the expected consideration to be received for all the goods and services we expect to provide. We update the transaction price for expected consideration, subject to constraint, each reporting period if our estimate of future goods to be ordered by customers change.

Research and Development Revenues

We perform research and development activities as specified in each respective customer agreement. We identify each performance obligation in our research and development agreements at contract inception. We allocate the consideration to each distinct performance obligation based on the estimated SSP of each performance obligation. Performance obligations included in our research and services agreements typically include research and development services for a specified term, periodic reports and small samples of enzyme produced.

The majority of our research and development agreements are based on a contractual rate per FTE working on the project. The underlying product that we develop for customers does not create an asset with an alternative use to us and the customer receives benefits as we perform the work towards completion. Thus, our performance obligations are generally satisfied over time as the service is performed. We utilize an appropriate method of measuring progress towards the completion of our performance obligations to determine the timing of revenue recognition. For each performance obligation that is satisfied over time, we recognize revenue using a single measure of progress, typically based on FTE hours incurred.

Our contracts frequently provide customers with rights to use or access our products or technology, along with other promises or performance obligations. Under ASC 606, we must first determine whether the license is distinct from other promises, such as our promise to perform research and development services. If we determine that the customer cannot benefit from the license without our services, the license will be accounted for as combined with the other performance obligations. If we determine that a license is distinct, we would recognize an allocable portion of the transaction price when the license is transferred to the customer, and the customer can use and benefit from it. We estimate the SSP for license rights by using a discounted cash flow method which includes the following key assumptions: the development timelines, revenue forecasts, commercialization expenses, discount rate, and the probability of technical and regulatory success. For licenses that have been previously sold to other customers, we use historical information to determine SSP.

At the inception of each arrangement that includes variable consideration such as development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Our CodeEvolver® platform technology transfer collaboration agreements typically include license fees, upfront fees, and variable consideration in the form of milestone payments, and sales or usage-based royalties. We have recognized revenues from our platform technology transfer agreements over time.

We also have an agreement under which we have granted a functional license to some elements of our biocatalyst technology. We will recognize revenues for the functional license at a point in time when the control of the license transfers to the customer.

For agreements that include sales or usage-based royalty payments to us for which the license is the predominant item to which the royalty relates, we do not recognize revenue until the underlying sales of the product or usage has

occurred. At the end of each reporting period, we estimate the royalty amount. We recognize revenue at the later of (i) when the related sale of the product occurs, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied, or partially satisfied.

We recognized revenues from a revenue sharing arrangement based upon sales of licensed products by our revenue sharing partner Exela PharmSci, Inc. (“Exela”) see Note 14 “Related Party Transactions” in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K. We recognized revenues net of product and selling costs

upon notification from our revenue sharing partner of our portion of net profit based on the contractual percentage from the sale of licensed product. The revenue sharing arrangement was terminated in December 2017.

Policy before January 1, 2018

We recognize revenue from the sale of our products, collaborative research and development agreements and revenue sharing arrangements. Revenue is recognized when the related costs are incurred and the four basic criteria of revenue recognition are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the fee is fixed or determinable; and (4) collectability is reasonably assured. Where the revenue recognition criteria are not met, we defer the recognition of revenue by recording deferred revenue until such time that all criteria of revenue recognition are met.

We account for revenues from multiple element arrangements, such as license and platform technology transfer agreements in which a licensee may purchase several deliverables, in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Subtopic 605-25, "Multiple Element Arrangements." For new or materially amended multiple element arrangements, we identify the deliverables at the inception of the arrangement and each deliverable within a multiple deliverable revenue arrangement is accounted for as a separate unit of accounting if both of the following criteria are met: (1) the delivered item or items have value to the customer on a standalone basis and (2) for an arrangement that includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control. Revenue allocated to each element is then recognized based on when the basic four revenue recognition criteria are met for each element.

Where a portion of non-refundable up-front fees or other payments received are allocated to continuing performance obligations under the terms of a collaborative arrangement, they are recorded as deferred revenue and recognized as revenue ratably over the term of our estimated performance period under the agreement or using the proportional performance method based on the ratio of the level of effort incurred to date compared to the total estimated level of effort required to complete our performance obligations under the agreement. Determining the total estimated level of effort required to complete all performance obligations requires management judgment and estimation including assumptions regarding the number of internal hours required to complete the project and external effort incurred. We determine the estimated performance periods, and they are periodically reviewed based on the progress of the related program. The effect of any change made to an estimated performance period and, therefore, to revenue recognized, would occur on a prospective basis in the period that the change was made.

Product Sales

Product sales consist of sales of protein catalysts, pharmaceutical intermediates, and Codex® Biocatalyst Panels and Kits. Product sales are recognized once passage of title and risk of loss has occurred and contractually specified acceptance criteria, if any, have been met, provided all other revenue recognition criteria have also been met. Shipping and handling costs charged to customers are recorded as revenue.

Research and Development Revenues

Collaborative research and development agreements typically provide us with multiple revenue streams, including: research services fees for full time employee ("FTE") research services, up-front license fees, technology access, contingent payments upon achievement of contractual criteria, and royalty fees based on the licensee's product sales or cost savings achieved by our customers.

We perform collaborative research and development activities as specified in each respective customer agreement. Payments for services received are not refundable. Certain research agreements are based on a contractual reimbursement rate per FTE working on the project. We recognize revenue from research services as those services are performed over the contractual performance periods. When up-front payments are combined with FTE services in a single unit of accounting, we recognize the up-front payments using the proportionate performance method of revenue recognition based upon the actual amount of research labor hours incurred relative to the amount of the total expected labor hours to be incurred by us, up to the amount of cash received. In cases where the planned levels of research services fluctuate substantially over the research term, we are required to make estimates of the total hours required to perform our obligations.

We recognize research and development revenues from non-refundable, up-front license fees or technology access payments that are not dependent on any future performance by us when such amounts are earned. If we have continuing obligations to perform under the arrangement, such fees are recorded as deferred revenues and recognized over the estimated period of continuing performance. Estimated performance periods are periodically reviewed based on the progress of the related program. The effect of any change made to an estimated performance period, and therefore to revenue recognized, would occur on a prospective basis in the period that the change was made.

A payment that is contingent upon the achievement of a substantive milestone is recognized in its entirety in the period in which the milestone is achieved. A milestone is an event (i) that can only be achieved based in whole or in part on either our performance or on the occurrence of a specific outcome resulting from our performance, (ii) for which there is, as of the date the arrangement is entered into, substantive uncertainty that the event will be achieved and (iii) results in additional payments being due to us. Milestones are considered substantive when the consideration earned from the achievement of the milestone (i) is commensurate with either our performance to achieve the milestone or the enhancement of the value of the item delivered as a result of a specific outcome resulting from its performance, (ii) relates solely to past performance and (iii) is reasonable relative to all deliverable and payment terms in the arrangement.

We recognize revenue from other contingent payments based on passage of time or when earned as the result of a customer’s performance in accordance with the contractual terms and when such payments can be reasonably estimated and collectability of such payments is reasonably assured.

We recognize revenue from royalties based on licensees’ sales of our products or products using our technologies. Royalties are recognized as earned in accordance with the contract terms when royalties from licensees can be reasonably estimated and collectability is reasonably assured. For the majority of our royalty revenue, estimates are made using notification of the sale of licensed products from the licensees.

Stock-Based Compensation

We use the Black-Scholes-Merton option pricing model to estimate the fair value of options granted under our equity incentive plans. The Black-Scholes-Merton option pricing model requires the use of assumptions, including the expected term of the award and the expected stock price volatility. The expected term is based on historical exercise behavior on similar awards, giving consideration to the contractual terms, vesting schedules and expectations of future employee behavior. We use historical volatility to estimate expected stock price volatility. The risk-free rate assumption is based on United States Treasury instruments whose terms are consistent with the expected term of the stock options. The expected dividend assumption is based on our history and expectation of dividend payouts.

Restricted Stock Units ("RSUs") and Restricted Stock Awards ("RSAs") are measured based on the fair market values of the underlying stock on the dates of grant. Performance based options ("PBOs") and performance-contingent restricted stock units ("PSUs") are measured using Black-Scholes-Merton option pricing model. The vesting of PBOs and PSUs awarded is conditioned upon the attainment of one or more performance objectives over a specified period and upon continued employment through the applicable vesting date. At the end of the performance period, shares of stock subject to the PBOs and PSUs vest based upon both the level of achievement of performance objectives within the performance period and continued employment through the applicable vesting date.

Stock-based compensation expense is calculated based on awards ultimately expected to vest and is reduced for estimated forfeitures at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The estimated annual forfeiture rates for stock options, RSUs, PSUs, PBOs, and RSAs are based on historical forfeiture experience.

The estimated fair value of stock options, RSUs and RSAs are expensed on a straight-line basis over the vesting term of the grant and the estimated fair value of PSUs and PBOs are expensed using an accelerated method over the term of the award once management has determined that it is probable that the performance objective will be achieved. Compensation expense is recorded over the requisite service period based on management's best estimate as to whether it is probable that the shares awarded are expected to vest. Management assesses the probability of the performance milestones being met on a continuous basis.

Impairment of Long-Lived Assets

We evaluate the carrying value of long-lived assets, including property and equipment, whenever events, changes in business circumstances or our planned use of long-lived assets indicate that their carrying amounts may not be fully recoverable or that their useful lives are no longer appropriate. If these facts and circumstances exist, we assess for recovery by comparing the carrying values of long-lived assets with their future net undiscounted cash flows. If the comparison indicates that impairment exists, long-lived assets are written down to their respective fair value based on discounted cash flows. Significant management judgment is required in the forecast of future operating results that are used in the preparation of expected undiscounted cash flows.

No impairment charges for long-lived assets were recorded during the year ended December 31, 2018, 2017 and 2016.

Goodwill

Goodwill represents the excess of the consideration transferred over the fair value of net assets of businesses acquired and is assigned to reporting units. We test goodwill for impairment considering amongst other things, whether there have been sustained declines in our share price. If we conclude it is more likely than not that the fair value of a reporting unit is less than its carrying amount, a quantitative fair value test is performed. In the first quarter of 2018, we determined that we operate in two segments and accordingly we re-evaluated our assessment of the number of reporting units. We concluded that we have two reporting units that reflect our operating segments and accordingly, we tested goodwill for impairment at the reporting unit level. Historically, assets are jointly used by the segments, are not separable, and are not identified by reporting unit. In order to assign the amount of goodwill to the two reporting units, we used a relative fair value allocation methodology that primarily relied on our estimates of revenue and future earnings for each reporting units. Using the relative fair value allocation methodology, we have determined that approximately 76% of goodwill is allocated to the Performance Enzymes segment and 24% is allocated to the Novel Biotherapeutics segment. As a result of the calculation, $2.4 million of the goodwill was assigned to the Performance Enzymes segment and $0.8 million was assigned to the Novel Biotherapeutics segment. There were no changes in the amount of goodwill assigned to each reporting unit at the end of the year. During 2018, 2017 and 2016, we did not record impairment charges related to goodwill.

Income Taxes

We use the liability method of accounting for income taxes, whereby deferred tax asset or liability account balances are calculated at the balance sheet date using current tax laws and rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are provided when necessary to reduce deferred tax assets to the amount that will more likely than not be realized.

We make certain estimates and judgments in determining income tax expense for financial statement purposes. These estimates and judgments occur in the calculation of tax credits, benefits and deductions and in the calculation of certain tax assets and liabilities, which arise from differences in the timing of recognition of revenues and expenses for tax and financial statement purposes. Significant changes to these estimates may result in an increase or decrease to our tax provision in a subsequent period.

In assessing the realizability of deferred tax assets, we consider whether it is more likely than not that some portion or all of the deferred tax assets will be realized on a jurisdiction by jurisdiction basis. The ultimate realization of deferred tax assets is dependent upon the generation of taxable income in the future. We have recorded a valuation allowance against these deferred tax assets in jurisdictions where ultimate realization of deferred tax assets is more likely than not to occur. As of December 31, 2018, we maintain a full valuation allowance in all jurisdictions against the net deferred tax assets as we believe that it is more likely than not that the majority of deferred tax assets will not be realized.

We make estimates and judgments about our future taxable income that are based on assumptions that are consistent with our plans and estimates. Should the actual amounts differ from our estimates, the amount of our valuation allowance may be materially impacted. Any adjustment to the deferred tax asset valuation allowance would be recorded in the statements of operations for the periods in which the adjustment is determined to be required.

We account for uncertainty in income taxes as required by the provisions of ASC Topic 740, which clarifies the accounting for uncertainty in income taxes recognized in an enterprise’s financial statements. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to estimate and measure the tax benefit as the largest amount that is more than 50% likely of being realized upon ultimate settlement. It is inherently difficult and subjective to estimate such amounts, as this requires us to determine the probability of various possible outcomes. We consider many factors when evaluating and estimating our tax positions and tax benefits, which may require periodic adjustments and may not accurately anticipate actual outcomes.

The Tax Reform Act of 1986 and similar state provisions limit the use of net operating loss (“NOL”) carryforwards in certain situations where equity transactions result in a change of ownership as defined by Internal Revenue Code Section 382. In the event we should experience such a change of ownership, utilization of our federal and state NOL

carryforwards could be limited. We performed an analysis in 2018 and determined that there was not a limitation that would result in the expiration of carryforwards before they are utilized.

The adoption of ASC 606 primarily resulted in less cumulative revenue recognized as of January 1, 2018, which in turn generated an increase in net deferred tax assets. As we fully reserve our net deferred tax assets in the jurisdictions impacted by the adoption of ASC 606, this impact was offset by a corresponding increase to the valuation allowance.

We maintain a full valuation allowance against net deferred tax assets as we believe that it is more likely than not that the majority of deferred tax assets will not be realized.

Changes to Tax Law

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 (the "Tax Act") was signed into law making significant changes to the Internal Revenue Code. The Tax Act made broad and complex changes to the U.S. tax code, including, but not limited to, (i) reducing the U.S. federal statutory tax rate from 35% to 21%; (ii) requiring companies to pay a one-time transition tax on certain un-repatriated earnings of foreign subsidiaries; (iii) generally eliminating U.S federal income taxes on dividends from foreign subsidiaries; (iv) requiring a current inclusion in U.S. federal taxable income of certain earnings of controlled foreign corporations; (v) eliminating the corporate alternative minimum tax ("AMT") and changing how existing AMT credits can be realized; (vi) creating the base erosion anti-abuse tax ("BEAT"), a new minimum tax; (vii) creating a tax on global intangible low-taxed income ("GILTI") of foreign subsidiaries; (viii) creating a new limitation on deductible interest expense; (ix) changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017; and (x) modifying the officer's compensation limitation.

In December 2017, the SEC issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provided a measurement period of up to one year from the enactment date of the Tax Act for companies to complete the accounting for the Tax Act and its related impacts. In 2018, we completed its accounting for the Tax Act. The income tax effects of the Tax Act for which the accounting is now completed include: the impact of the transition tax, the revaluation of deferred tax assets and liabilities to reflect the 21% corporate tax rate, and the impact to the aforementioned items on state income taxes. We have completed our accounting for the income tax effects under the Tax Act that are relevant to us and required to be recorded and disclosed pursuant to FASB ASC 740, Income Taxes. Accordingly, any and all provisional amounts previously recorded in accordance with SEC Staff Accounting Bulletin No. 118 have been adjusted to reflect their final amounts.

Because ASC 740-10-25-47 requires the effect of a change in tax laws or rates to be recognized as of the date of enactment, we remeasured our deferred tax assets and liabilities, and offsetting valuation allowance in 2017. There was no impact to tax expense as the remeasurement of net deferred tax assets was completely offset by a corresponding change in valuation allowance. The reduction to U.S. deferred tax assets and the offsetting valuation allowance was $34.1 million.

Beginning in 2018, the GILTI provisions in the Tax Act require us to include, in our U.S. income tax return, foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. Per guidance issued by the FASB, companies can either account for deferred taxes related to GILTI or treat tax arising from GILTI as a period cost. Both are acceptable methods subject to an accounting policy election. At December 31, 2018, we finalized our policy and have elected to use the period cost method for GILTI. In 2018, we did not incur any GILTI inclusion as our foreign subsidiaries generated losses.

The BEAT provisions in the Tax Act eliminate the deduction of certain base-erosion payments made to related foreign corporations, and impose a minimum base erosion anti-abuse tax if greater than regular tax. In 2018, our company was not subject to BEAT as it did not meet the requirements to be subject to BEAT.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Sensitivity

We had unrestricted cash and cash equivalents totaling $53.0 million at December 31, 2018. These amounts were invested primarily in money market funds and are held for working capital purposes. We do not enter into investments for trading or speculative purposes. We believe we do not have material exposure to changes in fair value as a result of changes in interest rates. Declines in interest rates, however, will reduce future investment income. If overall interest

rates fell by 10% in 2018, our results of operations and cash flows would not be materially affected.

Foreign Currency Risk

Our results of operations and cash flows are subject to fluctuations due to changes in foreign currency exchange rates. In periods when the United States dollar declines in value as compared to the foreign currencies in which we incur expenses, our foreign-currency based expenses increase when translated into United States dollars. Although substantially all of our sales are denominated in United States dollars, future fluctuations in the value of the United States dollar may affect the price

competitiveness of our products outside the United States. The effect of a 10% unfavorable change in exchange rates on foreign denominated receivables and cash as of December 31, 2018 would have had foreign exchange losses of approximately $0.1 million recognized as a component of other expense in our consolidated statement of operations. We did not engage in hedging transactions in 2018, 2017 and 2016.

Equity Price Risk

As described further in Note 6 to the Consolidated Financial Statements, we have an investment in common shares of CO_2 Solutions Inc., a company based in Quebec, Canada ("CO_2 Solutions"), whose shares are publicly traded in Canada on the TSX Venture Exchange. As of December 31, 2018, the fair value of our investment in CO_2 Solutions' common stock was $0.6 million.

This investment is exposed to fluctuations in both the market price of CO_2 Solutions' common shares and changes in the exchange rates between the United States dollar and the Canadian dollar. The effect of a 10% adverse change in the market price of CO_2 Solutions' common shares as of December 31, 2018 would have been a loss of approximately $0.1 million, recognized as a component of other expense in our consolidated statements of operations. The effect of a 10% unfavorable change in the exchange rates between the United States dollar and the Canadian dollar as of December 31, 2018 would have been a loss of approximately $0.1 million, recognized as a component of other expense in our consolidated statements of operations.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Codexis, Inc.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm
Shareholders and Board of Directors
Codexis, Inc.
Redwood City, California
Opinion on the Consolidated Financial Statements
We have audited the accompanying consolidated balance sheets of Codexis, Inc. (the “Company”) and subsidiaries as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, stockholders’ equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company and subsidiaries at December 31, 2018 and 2017, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.
We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (“PCAOB”), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (“COSO”) and our report dated March 1, 2019 expressed an unqualified opinion thereon.

Change in Accounting Principle
As discussed in Notes 2 and 3 to the consolidated financial statements, the Company has changed its accounting method for recognizing revenue from contracts with customers in fiscal year 2018 due to the adoption of Topic 606: Revenue from Contracts with Customers.
Basis for Opinion
These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s consolidated financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.
We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.
Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP
We have served as the Company's auditor since 2013.
San Jose, California
March 1, 2019

Report of Independent Registered Public Accounting Firm
Shareholders and Board of Directors
Codexis, Inc.
Redwood City, California
Opinion on Internal Control over Financial Reporting
We have audited Codexis, Inc.'s (the "Company's") internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO criteria"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.
We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company and subsidiaries as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2018 and the related notes, and our report dated March 1, 2019 expressed an unqualified opinion thereon.
Basis for Opinion
The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying "Item 9A, Management's Report on Internal Control over Financial Reporting". Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.
We conducted our audit of internal control over financial reporting in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.
Definition and Limitations of Internal Control over Financial Reporting
A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.
Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ BDO USA, LLP
San Jose, California
March 1, 2019

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Codexis, Inc.
Consolidated Balance Sheets
(In Thousands, Except Per Share Amounts)

	December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$53,039	$31,219
Accounts receivable, net of allowances of $34 at December 31, 2018 and 2017	11,551	11,447
Unbilled receivables, current	1,916	353
Inventories	589	1,036
Prepaid expenses and other current assets	1,068	984
Contract assets	35	—
Total current assets	68,198	45,039
Restricted cash	1,446	1,557
Equity securities	588	671
Property and equipment, net	4,759	2,815
Goodwill	3,241	3,241
Other non-current assets	1,051	302
Total assets	$79,283	$53,625
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$3,050	$3,545
Accrued compensation	5,272	4,753
Other accrued liabilities	4,855	4,362
Deferred revenue	4,936	12,292
Total current liabilities	18,113	24,952
Deferred revenue, net of current portion	3,352	1,501
Lease incentive obligation, net of current portion	35	460
Capital lease obligation, net of current portion	61	302
Other long-term liabilities	1,416	1,863
Total liabilities	22,977	29,078
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.0001 par value per share; 5,000 shares authorized, none issued and outstanding	—	—
Common stock, $0.0001 par value per share; 100,000 shares authorized; 54,065 and 48,365 shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively	5	5
Additional paid-in capital	386,775	340,079
Accumulated other comprehensive loss	—	(472)
Accumulated deficit	(330,474)	(315,065)
Total stockholders' equity	56,306	24,547
Total liabilities and stockholders' equity	$79,283	$53,625

See Accompanying Notes to Consolidated Financial Statements

Codexis, Inc.
Consolidated Statements of Operations
(In Thousands, Except Per Share Amounts)

	Year Ended December 31,		
	2018	2017	2016
Revenues:			
Product revenue	$25,590	$26,685	$15,321
Research and development revenue	35,004	23,339	33,516
Total revenues	60,594	50,024	48,837
Costs and operating expenses:			
Cost of product revenue	12,620	14,327	9,753
Research and development	29,978	29,659	22,229
Selling, general and administrative	29,291	29,008	25,419
Total costs and operating expenses	71,889	72,994	57,401
Loss from operations	(11,295)	(22,970)	(8,564)
Interest income	671	147	60
Other expenses, net	(291)	(92)	(94)
Loss before income taxes	(10,915)	(22,915)	(8,598)
Provision for (benefit from) income taxes	(37)	81	(40)
Net loss	$(10,878)	$(22,996)	$(8,558)
Net loss per share, basic and diluted	$(0.21)	$(0.50)	$(0.21)
Weighted average common stock shares used in computing net loss per share, basic and diluted	52,205	46,228	40,629

See Accompanying Notes to Consolidated Financial Statements

Codexis, Inc.
Consolidated Statements of Comprehensive Loss
(In Thousands)

	Year Ended December 31,		
	2018	2017	2016
Net loss	$(10,878)	$(22,996)	$(8,558)
Other comprehensive loss:			
Unrealized loss on equity securities, net of tax [1]	—	(472)	(405)
Other comprehensive loss	—	(472)	(405)
Total comprehensive loss	$(10,878)	$(23,468)	$(8,963)

[1] In 2018, we adopted Accounting Standards Update No. 2016-01 (Subtopic 825-10) and recorded a cumulative-effect reclassification $0.5 million unrealized loss on equity securities from other accumulated comprehensive loss to the beginning accumulated deficit. See Note 2 “Summary of Significant Accounting Policies” in the Accompanying Notes to the Consolidated Financial Statements for more information.

See Accompanying Notes to Consolidated Financial Statements

Codexis, Inc.
Consolidated Statements of Stockholders' Equity
(In Thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
December 31, 2015	40,343	$ 4	$305,981	$ 405	$(283,511)	$ 22,879
Exercise of stock options	398	—	1,034	—	—	1,034
Release of stock awards	911	—	—	—	—	—
Employee stock-based compensation	—	—	5,673	—	—	5,673
Taxes paid related to net share settlement of equity awards	(397)	—	(1,524)	—	—	(1,524)
Total comprehensive loss	—	—	—	(405)	(8,558)	(8,963)
December 31, 2016	41,255	4	311,164	—	(292,069)	19,099
Exercise of stock options	86	—	266	—	—	266
Release of stock awards	1,096	—	—	—	—	—
Employee stock-based compensation	—	—	7,048	—	—	7,048
Non-employee stock-based compensation	—	—	43	—	—	43
Taxes paid related to net share settlement of equity awards	(397)	—	(1,670)	—	—	(1,670)
Issuance of common stock, net of issuance costs	6,325	1	23,228	—	—	23,229
Total comprehensive loss	—	—	—	(472)	(22,996)	(23,468)
December 31, 2017	48,365	5	340,079	(472)	(315,065)	24,547
Exercise of stock options	856	—	4,680	—	—	4,680
Release of stock awards	832	—	—	—	—	—
Employee stock-based compensation	—	—	7,865	—	—	7,865
Non-employee stock-based compensation	—	—	24	—	—	24
Taxes paid related to net share settlement of equity awards	(301)	—	(3,190)	—	—	(3,190)
Issuance of common stock, net of issuance costs	4,313	—	37,317	—	—	37,317
Cumulative effect of change in accounting principles [1]	—	—	—	472	(4,531)	(4,059)
Net Loss	—	—	—	—	(10,878)	$(10,878)
December 31, 2018	54,065	$ 5	$386,775	$ —	$(330,474)	$ 56,306

[1] Cumulative effect of change in accounting principles includes: Accounting Standards Update 2014-9 (Topic 606), of $4.1 million and Accounting Standards Update 2016-01 (Subtopic 825-10), of $0.5 million. See Note 2 "Summary of Significant Accounting Policies" in the Accompanying Notes to the Consolidated Financial Statements for more information.

See Accompanying Notes to Consolidated Financial Statements

Codexis, Inc.
Consolidated Statements of Cash Flows
(In Thousands)

	Year Ended December 31,		
	2018	2017	2016
Operating activities:			
Net loss	$(10,878)	$(22,996)	$(8,558)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization of intangible assets	—	—	2,812
Depreciation	1,147	1,042	1,734
Stock-based compensation	7,889	7,091	5,673
Loss (gain) on disposal of property and equipment	8	9	(42)
Loss on investment securities	83	—	—
Gain from extinguishment of asset retirement obligation	—	(207)	—
Changes in operating assets and liabilities:			
Accounts receivable, net	960	(5,298)	1,405
Inventories	447	(210)	167
Prepaid expenses and other current assets	(37)	157	7
Contract assets	(35)	—	—
Unbilled receivables	(2,349)	(353)	—
Other non-current assets	228	(44)	52
Accounts payable	(524)	(801)	942
Accrued compensation	519	439	983
Other accrued liabilities	(17)	1,399	(593)
Other long-term liabilities	(904)	—	—
Deferred revenue	(10,631)	11,017	(6,442)
Net cash used in operating activities	(14,094)	(8,755)	(1,860)
Investing activities:			
Purchase of property and equipment	(2,768)	(985)	(888)
Proceeds from disposal of property and equipment	2	2	42
Net cash used in investing activities	(2,766)	(983)	(846)
Financing activities:			
Proceeds from exercises of stock options	4,680	266	1,034
Proceeds from issuance of common stock in connection with public offering, net of underwriting discounts and commission	37,497	23,782	—
Costs incurred in connection with public offering	(180)	(553)	—
Principal payments on capital lease obligations	(238)	(175)	—
Taxes paid related to net share settlement of equity awards	(3,190)	(1,670)	(1,524)
Net cash provided by (used in) financing activities	38,569	21,650	(490)
Net increase (decrease) in cash, cash equivalents and restricted cash	21,709	11,912	(3,196)
Cash, cash equivalents and restricted cash at the beginning of the year	32,776	20,864	24,060
Cash, cash equivalents and restricted cash at the end of the year	$54,485	$32,776	$20,864
Supplemental disclosure of cash flow information:			
Interest paid	$84	$141	$14
Income taxes	$5	$32	$5
Supplemental non-cash financing activities:			
Equipment acquired under capital leases	$—	$862	$—
Capital expenditures incurred but not yet paid	$300	$42	$125

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheets to the total of the same such amounts shown above (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Cash and cash equivalents	$53,039	$31,219	$19,240
Restricted cash included in non-current assets	1,446	1,557	1,624
Total cash, cash equivalents and restricted cash at the end of the period	$54,485	$32,776	$20,864

See Accompanying Notes to Consolidated Financial Statements

Codexis, Inc.
Notes to Consolidated Financial Statements
Note 1. Description of Business
In these notes to the consolidated financial statements, the “Company,” “we,” “us,’” and “our” refers to Codexis, Inc. and its subsidiaries on a consolidated basis.
We discover, develop and sell proteins that deliver value to our clients in a growing set of industries. We view proteins as a vast untapped source of value-creating materials, and we are using our proven technologies, which have been continuously improved over our fifteen year history, to commercialize an increasing number of novel proteins, both as proprietary Codexis products and in partnership with our customers.
We are a pioneer in the harnessing of computational technologies to drive biology advancements. Over the last fifteen years, we have made substantial investments in the development of our CodeEvolver® protein engineering technology platform, the primary source of our competitive advantage. Our technology platform is powered by proprietary, artificial intelligence-based, computational algorithms that rapidly mine our large and continuously growing library of protein variants’ performance attributes. These computational outputs enable increasingly reliable predictions for next generation protein variants to be engineered, enabling delivery of targeted performance enhancements in a time-efficient manner. In addition to its computational prowess, our CodeEvolver® protein engineering technology platform integrates additional modular competencies, including robotic high-throughput screening and genomic sequencing, organic chemistry and process development which are all coordinated to create our novel protein innovations.
Our approach to developing commercially viable biocatalytic manufacturing processes begins by conceptually designing the most cost-effective and practical process for a targeted product. We then develop optimized protein catalysts to enable that process design, using our CodeEvolver® protein engineering platform technology. Engineered protein catalyst candidates - many thousands for each protein engineering project - are then rapidly screened and validated in high throughput screening under relevant manufacturing operating conditions. This approach results in an optimized protein catalyst enabling cost-efficient processes that typically are relatively simple to run in conventional manufacturing equipment. This also allows for the efficient technical transfer of our process to our manufacturing partners.
The successful embodiment of our CodeEvolver® protein engineering technology platform in commercial manufacturing processes requires well-integrated expertise in a number of technical disciplines. In addition to those directly involved in practicing our CodeEvolver® protein engineering platform technology, such as molecular biology, enzymology, microbiology, cellular engineering, metabolic engineering, bioinformatics, biochemistry and high throughput analytical chemistry, our process development projects also involve integrated expertise in organic chemistry, chemical process development, chemical engineering, fermentation process development and fermentation engineering. Our integrated, multi-disciplinary approach to biocatalyst and process development is a critical success factor for our company.
We initially commercialized our CodeEvolver® protein engineering technology platform and products in the pharmaceuticals market, which remains our primary business focus. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development.
We have also used the technology to develop protein catalysts for use in the fine chemicals market. The fine chemicals market consists of several large market verticals, including food and food ingredients, animal feed, flavors, fragrances, and agricultural chemicals.
We have also begun using the CodeEvolver® protein engineering technology platform to develop early stage, novel biotherapeutic product candidates, both for our customers and for our own business, most notably our lead program for the potential treatment of PKU in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we entered into a Global Development, Option and License Agreement with Nestec, Ltd. (“Nestlé Health Science”) to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license to develop and commercialize CDX-6114.

In April 2018, we entered into a strategic agreement (the "Porton Agreement") with Porton Pharma Solutions, Ltd. ("Porton") to license key elements of our platform technology to Porton’s global custom intermediate and active pharmaceutical ingredients ("API") development and manufacturing business. This gives us access to a wide variety of small and medium-sized pharmaceutical customers.

We are also using our technology to develop enzymes for customers using next generation sequencing ("NGS") and polymerase chain reaction ("PCR/qPCR") for in vitro molecular diagnostic and genomic research applications. Our first enzyme is a ligase which we began marketing to customers in 2018.

Below are brief descriptions of our business segments:

Performance Enzymes

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the pharmaceuticals market, and to date this continues to be our largest market served. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. We have also used the technology to develop customized enzymes for use in other industrial markets. These markets consist of several large industrial verticals, including food and food ingredients, animal feed, flavors, fragrances, and agricultural chemicals. We also use our technology to develop enzymes for customers using NGS and PCR/qPCR for in vitro molecular diagnostic and molecular biology research applications. In April 2018, we entered into the Porton Agreement related to our strategic collaboration with Porton to license key elements of our world-leading biocatalyst technology for use in Porton's global custom intermediate and API development and manufacturing business.

Novel Biotherapeutics

We are also targeting new opportunities in the pharmaceutical industry to discover, improve, and/or develop biotherapeutic drug candidates. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity. Most notable is our lead program for the potential treatment of hyperphenylalaninemia ("HPA") (also referred to as PKU) in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we announced a strategic collaboration with Nestlé Health Science to advance CDX-6114, our own novel orally administrable enzyme therapeutic candidate for the potential treatment of PKU. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, which was conducted in Australia. In November 2018, we announced top-line results from the Phase 1a study in healthy volunteers with CDX-6114. In December 2018, Nestlé Health Science became obligated to pay us an additional $1.0 million within 60 days after the achievement of a milestone relating to formulation of CDX-6114. In January 2019, we received notice from the U.S. Food and Drug Administration (the "FDA") that it had completed its review of our investigational new drug application ("IND") for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, Nestlé Health Science is obligated to pay us $3.0 million within 60 days after exercise of the option. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, "Subsequent Events" for additional details. Other potential payments from Nestlé Health Science to us under the Nestlé Agreement include (i) development and approval milestones of up to $86.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of Product.

We have also developed a pipeline of other biotherapeutic drug candidates in which we expect to continue to make additional investments with the aim of advancing additional product candidates targeting other therapeutic areas.

For additional discussion of our business segments, see Note 15, "Segment, Geographical and Other Revenue Information."

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Note 2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America (“GAAP”) and the applicable rules and regulations of the Securities and Exchange Commission (“SEC”) and include the accounts of Codexis, Inc. and its wholly-owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Comprehensive income or loss

Comprehensive loss is equivalent to net loss in 2018 because after adopting Accounting Standards Update No. 2016-01, "Financial Instruments-Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities." (“Subtopic 825-10”), we do not have any other transactions recorded under comprehensive loss. Prior to our adoption of Subtopic 825-10, and for the year ended in December 31, 2017 and 2016, comprehensive loss included unrealized gains and unrealized losses from our equity investment in equity securities. See “Recently adopted accounting pronouncements” below for additional information.

Certain prior year amounts have been reclassified to conform to 2018 presentation. These changes and reclassifications did not impact net loss or comprehensive loss.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosures of contingent liabilities at the date of the consolidated financial statements, and the reported amounts of revenue and expenses during the reporting period. We regularly assess these estimates which primarily affect revenue recognition, accounts receivable, inventories, the valuation of equity securities, goodwill arising out of business acquisitions, accrued liabilities, stock awards and the valuation allowances associated with deferred tax assets. Actual results could differ from those estimates and such differences may be material to the consolidated financial statements.

Segment Reporting

We report two business segments, Performance Enzymes and Novel Biotherapeutics, which are based on our operating segments. Operating segments are defined as components of an enterprise about which separate financial information is available that is evaluated regularly by the chief operating decision maker ("CODM"), or decision making group, in deciding how to allocate resources, and in assessing performance. Our CODM is our Chief Executive Officer. Our business segments are primarily based on our organizational structure and our operating results as used by our CODM in assessing performance and allocating resources for our company. We do not allocate or evaluate assets by segment.

Previously, we had only one business segment. As our biotherapeutics business has emerged as a significant opportunity for us, effective in 2018, we formed Novel Biotherapeutics as a new business segment. The Novel Biotherapeutics segment focuses on new opportunities in the pharmaceutical industry to discover or improve novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. The Performance Enzymes segment consists of the existing protein catalyst products and services with focus on pharmaceutical, food, molecular diagnostics, and other industrial markets.

Foreign Currency Translation

The United States dollar is the functional currency for our operations outside the United States. Accordingly, nonmonetary assets and liabilities originally acquired or assumed in other currencies are recorded in United States dollars at the exchange rates in effect at the date they were acquired or assumed. Monetary assets and liabilities denominated in other currencies are translated into United States dollars at the exchange rates in effect at the balance sheet date. Translation adjustments are recorded in other expense in the consolidated statements of operations. Gains and losses realized from non-U.S. dollar transactions, including intercompany balances not considered as permanent investments, denominated in currencies other than an entity’s functional currency are included in other expense in the accompanying consolidated statements of operations.

Revenue Recognition

Policy from January 1, 2018

On January 1, 2018, we adopted the provisions of Accounting Standards Update (ASU) 2014-09, "Revenue from Contracts with Customers (Topic 606) and the related amendments (“ASC 606”). The guidance provides a unified model to determine how revenue is recognized.

Our revenues are derived primarily from product revenue and collaborative research and development agreements. The majority of our contracts with customers typically contain multiple products and services. We account for individual products and services separately if they are distinct-that is, if a product or service is separately identifiable from other items in the contract and if a customer can benefit from it on its own or with other resources that are readily available to the customer.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our product revenue and collaborative research and development agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

The majority of our collaborative contracts contain multiple revenue streams such as up-front and/or annual license fees, fees for full time employee ("FTE") research and development services, contingent milestone payments upon achievement of contractual criteria, and royalty fees based on the licensees' product revenue or usage, among others. We determine the stand-alone selling price ("SSP") and allocate consideration to distinct performance obligations. Typically, we base our SSPs on our historical sales. If an SSP is not directly observable, then we estimate the SSP taking into consideration market conditions, forecasted sales, entity-specific factors and available information about the customer. We estimate the SSP for license rights by using a discounted cash flow method which includes the following key assumptions: the development timelines, revenue forecasts, commercialization expenses, discount rate, and the probability of technical and regulatory success. For licenses that have been previously sold to other customers, we use historical information to determine SSP.

We account for a contract with a customer when there is approval and commitment from both parties, the rights of the parties are identified, payment terms are identified, the contract has commercial substance and collectability of consideration is probable. Non-cancellable purchase orders received from customers to deliver a specific quantity of product, when combined with our order confirmation, in exchange for future consideration, create enforceable rights and obligations on both parties and constitute a contract with a customer.

We measure revenue based on the consideration specified in the contract with each customer, net of any sales incentives and taxes collected on behalf of government authorities. We recognize revenue in a manner that best depicts the transfer of promised goods or services to the customer, when control of the product or service is transferred to a customer. We make significant judgments when determining the appropriate timing of revenue recognition.

The following is a description of principal activities from which we generate revenue:

Product Revenue

Product revenue consist of sales of protein catalysts, pharmaceutical intermediates and Codex® Biocatalyst Panels and Kits. A majority of our product revenue is made pursuant to purchase orders or supply agreements and is recognized at a point in time when the control of the product has been transferred to the customer typically upon shipment. For some of the products that we develop, we recognize revenue over time as the product is manufactured because we have a right to payment from the customer under a binding, non-cancellable purchase order, and there is no alternate use of the product for us as it is specifically made for the customer’s use.

Certain of our agreements provide options to customers which they can exercise at a future date, such as the option to purchase our product during the contract duration at discounted prices and an option to extend their contract, among others. In accounting for customer options, we determine whether an option is a material right and this requires us to exercise significant judgment. If a contract provides the customer an option to acquire additional goods or services at a discount that exceeds the range of discounts that we typically give for that product or service for the same class of

customer, or if the option provides the customer certain additional goods or services for free, the option may be considered a material right. If the contract gives the customer the option to acquire additional goods or services at their normal SSPs, we would likely determine that the option is not a material right and, therefore, account for it as a separate performance obligation when the customer exercises the option. We primarily account for options which provide material rights using the alternative approach available under ASC 606, as we

concluded we meet the criteria for using the alternative approach. Therefore, the transaction price is calculated as the expected consideration to be received for all the goods and services we expect to provide under the contract. We update the transaction price for expected consideration, subject to constraint, each reporting period if our estimate of future goods to be ordered by customers change.

Research and Development Revenues

We perform research and development activities as specified in each respective customer agreement. We identify each performance obligation in our research and development agreements at contract inception. We allocate the consideration to each distinct performance obligation based on the estimated SSP of each performance obligation. Performance obligations included in our research and services agreements typically include research and development services for a specified term, periodic reports and small samples of enzyme produced.

The majority of our research and development agreements are based on a contractual rate per FTE working on the project. The underlying product that we develop for customers does not create an asset with an alternative use to us and the customer receives benefits as we perform the work towards completion. Thus, our performance obligations are generally satisfied over time as the service is performed. We utilize an appropriate method of measuring progress towards the completion of our performance obligations to determine the timing of revenue recognition. For each performance obligation that is satisfied over time, we recognize revenue using a single measure of progress, typically based on FTE hours incurred.

Our contracts frequently provide customers with rights to use or access our products or technology, along with other promises or performance obligations. Under ASC 606, we must first determine whether the license is distinct from other promises, such as our promise to manufacture a product. If we determine that the customer cannot benefit from the license without our manufacturing capability, the license will be accounted for as combined with the other performance obligations. If we determine that a license is distinct and has significant standalone functionality, we would recognize revenues from a functional license at a point in time when the license is transferred to the customer, and the customer can use and benefit from it. We estimate the SSP for license rights by using a discounted cash flow method which includes the following key assumptions: the development timelines, revenue forecasts, commercialization expenses, discount rate, and the probability of technical and regulatory success. For licenses that have been previously sold to other customers, we use historical information to determine SSP.

At the inception of each arrangement that includes variable consideration such as development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Our CodeEvolver® platform technology transfer collaboration agreements typically include license fees, upfront fees, and variable consideration in the form of milestone payments, and sales or usage-based royalties. We have recognized revenues from our platform technology transfer agreements over time as our customer learns to use our technology. We also have an agreement under which we have granted a functional license to some elements of our biocatalyst technology. We recognize revenues for the functional license at a point in time when the control of the license and technology transfers to the customer.

For agreements that include sales or usage-based royalty payments to us, we do not recognize revenue until the underlying sales of the product or usage has occurred. At the end of each reporting period, we estimate the royalty amount. We recognize revenue at the later of (i) when the related sale of the product occurs, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied, or partially satisfied.

Contract Assets

Contract assets include amounts related to our contractual right to consideration for completed performance obligations not yet invoiced. The contract assets are reclassified to receivables when the rights become unconditional.

Contract Liabilities

Contract liabilities are recorded as deferred revenues and include payments received in advance of performance under the contract. Contract liabilities are realized when the development services are provided to the customer or control of the products has been transferred to the customer. A portion of our contract liabilities relate to supply arrangements that contain material rights that are recognized using the alternative method, under which the aggregate amount invoiced to the customer for shipped products, including annual fees, is higher than the amount of revenue recognized based on the transaction price allocated to the shipped products.

Contract Costs

ASC 606 requires the recognition of an asset for the incremental costs of obtaining a contract with a customer if the entity expects to recover such costs. Incremental costs are costs that would not have been incurred if the contract had not been obtained. Examples of contract costs are commissions paid to sales personnel. We do not typically incur significant incremental costs because the compensation of our salespeople are not based on contracts closed but on a mixture of company goals, individual goals, and sales goals. If a commission paid is directly related to obtaining a specific contract, our policy is to capitalize and amortize such costs on a systematic basis, consistent with the pattern of transfer of the good or service to which the asset relates.

Contract costs are reported in other non-current assets.

Revenue Recognition Policy before January 1, 2018

We recognize revenue from the sale of our products, collaborative research and development agreements and revenue sharing arrangements. Revenue is recognized when the related costs are incurred and the four basic criteria of revenue recognition are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the fee is fixed or determinable; and (4) collectability is reasonably assured. Where the revenue recognition criteria are not met, we defer the recognition of revenue by recording deferred revenue until such time that all criteria of revenue recognition are met.

We account for revenues from multiple element arrangements, such as license and platform technology transfer agreements in which a licensee may purchase several deliverables, in accordance with Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) Subtopic 605-25, “Multiple Element Arrangements.” For new or materially amended multiple element arrangements, we identify the deliverables at the inception of the arrangement and each deliverable within a multiple deliverable revenue arrangement is accounted for as a separate unit of accounting if both of the following criteria are met: (1) the delivered item or items have value to the customer on a standalone basis and (2) for an arrangement that includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control. Revenue allocated to each element is then recognized based on when the basic four revenue recognition criteria are met for each element.

Where a portion of non-refundable up-front fees or other payments received are allocated to continuing performance obligations under the terms of a collaborative arrangement, they are recorded as deferred revenue and recognized as revenue ratably over the term of our estimated performance period under the agreement or using the proportional performance method based on the ratio of the level of effort incurred to date compared to the total estimated level of effort required to complete our performance obligations under the agreement. Determining the total estimated level of effort required to complete all performance obligations requires management judgment and estimation including assumptions regarding the number of internal hours required to complete the project and external effort incurred. We determine the estimated performance periods, and they are periodically reviewed based on the progress of the related program. The effect of any change made to an estimated performance period and, therefore, to revenue recognized, would occur on a prospective basis in the period that the change was made.

Product Sales

Product sales consist of sales of protein catalysts, pharmaceutical intermediates, and Codex® Biocatalyst Panels and Kits. Product sales are recognized once passage of title and risk of loss has occurred and contractually specified acceptance criteria, if any, have been met, provided all other revenue recognition criteria have also been met. Shipping and handling costs charged to customers are recorded as revenue.

Research and Development Revenues

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Collaborative research and development agreements typically provide us with multiple revenue streams, including: research services fees for full time employee ("FTE") research services, up-front license fees, technology access, contingent payments upon achievement of contractual criteria, and royalty fees based on the licensee's product sales or cost savings achieved by our customers.

We perform collaborative research and development activities as specified in each respective customer agreement. Payments for services received are not refundable. Certain research agreements are based on a contractual reimbursement rate per FTE working on the project. We recognize revenue from research services as those services are performed over the contractual performance periods. When up-front payments are combined with FTE services in a single unit of accounting, we recognize the up-front payments using the proportionate performance method of revenue recognition based upon the actual amount of research labor hours incurred relative to the amount of the total expected labor hours to be incurred by us, up to the amount of cash received. In cases where the planned levels of research services fluctuate substantially over the research term, we are required to make estimates of the total hours required to perform our obligations.

We recognize research and development revenues from non-refundable, up-front license fees or technology access payments that are not dependent on any future performance by us when such amounts are earned. If we have continuing obligations to perform under the arrangement, such fees are recorded as deferred revenues and recognized over the estimated period of continuing performance. Estimated performance periods are periodically reviewed based on the progress of the related program. The effect of any change made to an estimated performance period, and therefore to revenue recognized, would occur on a prospective basis in the period that the change was made.

A payment that is contingent upon the achievement of a substantive milestone is recognized in its entirety in the period in which the milestone is achieved. A milestone is an event (i) that can only be achieved based in whole or in part on either our performance or on the occurrence of a specific outcome resulting from our performance, (ii) for which there is, as of the date the arrangement is entered into, substantive uncertainty that the event will be achieved and (iii) results in additional payments being due to us. Milestones are considered substantive when the consideration earned from the achievement of the milestone (i) is commensurate with either our performance to achieve the milestone or the enhancement of the value of the item delivered as a result of a specific outcome resulting from its performance, (ii) relates solely to past performance and (iii) is reasonable relative to all deliverable and payment terms in the arrangement.

We recognize revenue from other contingent payments based on passage of time or when earned as the result of a customer's performance in accordance with the contractual terms and when such payments can be reasonably estimated and collectability of such payments is reasonably assured.

We recognize revenue from royalties based on licensees' sales of our products or products using our technologies. Royalties are recognized as earned in accordance with the contract terms when royalties from licensees can be reasonably estimated and collectability is reasonably assured. For the majority of our royalty revenue, estimates are made using notification of the sale of licensed products from the licensees.

Cost of Product Revenue

Cost of product revenue comprises both internal and third party fixed and variable costs including materials and supplies, labor, facilities, and other overhead costs associated with our product sales. Shipping costs are included in our cost of product revenue. Such charges were not significant in any of the periods presented.

Fulfillment costs, such as shipping and handling, are recognized at a point in time and are included in cost of product sales.

Cost of Research and Development Services

Cost of research and development services related to FTE services under research and development agreements approximate the research funding over the term of the respective agreements and is included in research and development expense. Costs of services provided under license and platform technology transfer agreements are included in research and development expenses and are expensed in the periods in which such costs are incurred.

Research and Development Expenses

Research and development expenses consist of costs incurred for internal projects and partner-funded collaborative research and development activities, as well as license and platform technology transfer agreements, as mentioned

above. These costs include our direct and research-related overhead expenses, which include salaries and other personnel-related expenses (including stock-based compensation), occupancy-related costs, supplies, and depreciation of facilities and laboratory

equipment, as well as external costs, and are expensed as incurred. Costs to acquire technologies that are utilized in research and development and that have no alternative future use are expensed when incurred.

Advertising

Advertising costs are expensed as incurred and included in selling, general and administrative expenses in the consolidated statements of operations. Advertising costs were $0.5 million in 2018, $0.7 million in 2017 and $0.5 million in 2016.

Stock-Based Compensation

We use the Black-Scholes-Merton option pricing model to estimate the fair value of options granted under our equity incentive plans. The Black-Scholes-Merton option pricing model requires the use of assumptions, including the expected term of the award and the expected stock price volatility. The expected term is based on historical exercise behavior on similar awards, giving consideration to the contractual terms, vesting schedules and expectations of future employee behavior. We use historical volatility to estimate expected stock price volatility. The risk-free rate assumption is based on United States Treasury instruments whose terms are consistent with the expected term of the stock options. The expected dividend assumption is based on our history and expectation of dividend payouts. Restricted Stock Units ("RSUs") and Restricted Stock Awards ("RSAs") are measured based on the fair market values of the underlying stock on the dates of grant. Performance based options ("PBOs") and performance-contingent restricted stock units ("PSUs") are measured using Black-Scholes-Merton option pricing model. The vesting of PBOs and PSUs awarded is conditioned upon the attainment of one or more performance objectives over a specified period and upon continued employment through the applicable vesting date. At the end of the performance period, shares of stock subject to the PBOs and PSUs vest based upon both the level of achievement of performance objectives within the performance period and continued employment through the applicable vesting date.

Stock-based compensation expense is calculated based on awards ultimately expected to vest and is reduced for estimated forfeitures at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The estimated annual forfeiture rates for stock options, RSUs, PSUs, PBOs, and RSAs are based on historical forfeiture experience.

The estimated fair value of stock options, RSUs and RSAs are expensed on a straight-line basis over the vesting term of the grant and the estimated fair value of PSUs and PBOs are expensed using an accelerated method over the term of the award once management has determined that it is probable that the performance objective will be achieved. Compensation expense is recorded over the requisite service period based on management's best estimate as to whether it is probable that the shares awarded are expected to vest. Management assesses the probability of the performance milestones being met on a continuous basis.

Cash and Cash Equivalents

We consider all highly liquid investments with maturity dates of three months or less at the date of purchase to be cash equivalents. Cash and cash equivalents consist of cash on deposit with banks and money market funds. The majority of cash and cash equivalents is maintained with major financial institutions in the United States. Deposits with these financial institutions may exceed the amount of insurance provided on such deposits. Cash and cash equivalents totaled $53.0 million and comprised of cash of $21.8 million and money market funds of $31.2 million at December 31, 2018. Cash and cash equivalents totaled $31.2 million, comprised of cash of $24.4 million and money market funds of $6.8 million at December 31, 2017.

Restricted Cash

In 2016, we began the process of liquidating our Indian subsidiary. The local legal requirements for liquidation required us to maintain our subsidiary's cash balance in an account managed by a legal trustee to satisfy our financial obligations. This balance is recorded as non-current restricted cash on the consolidated balance sheets and totaled $0.7 million at December 31, 2018 and $0.8 million at December 31, 2017.

Pursuant to the terms of a lease agreement for our Redwood City, CA facilities, we obtained a letter of credit collateralized by cash deposit balances of $0.7 million as of December 31, 2018 and $0.8 million at December 31, 2017. These cash deposit balances are recorded as non-current restricted cash on the consolidated balance sheets. See Note 13, “Commitments and Contingencies”. In January 2019, we entered into the Eighth Amendment to the Lease for our Redwood City, CA facilities and,

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as a result, our letters of credit will be collateralized by a cash deposit balance of $1.1 million in 2019. See Note 16, “Subsequent Events” for additional information.

Equity Securities

We invest in equity securities that are carried at estimated fair value with changes in fair value recognized within earnings. Equity securities with remaining maturities of greater than one year or which we currently do not intend to sell are classified as long-term. See Note 6, “Cash Equivalents and Equity Securities.”

Unrealized holding gains and losses (the adjustment to fair value) and realized gains and losses are included in other income (expense) in the consolidated statement of operations subsequent to the adoption of ASU 2016-01 starting on January 1, 2018.

Fair Value Measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. In determining fair value, we utilize valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible and we consider counterparty credit risk in our assessment of fair value. Carrying amounts of financial instruments, including cash equivalents, accounts receivable, accounts payable, and accrued liabilities, approximate their fair values as of the balance sheet dates because of their short maturities.

The fair value hierarchy distinguishes between (1) market participant assumptions developed based on market data obtained from independent sources (observable inputs) and (2) an entity’s own assumptions about market participant assumptions developed based on the best information available in the circumstances (unobservable inputs). The fair value hierarchy consists of three broad levels, giving the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1) and the lowest priority to unobservable inputs (Level 3). The three levels of the fair value hierarchy are described below:

- Level 1: Inputs that are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.
- Level 2: Inputs that are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument’s anticipated life.
- Level 3: Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities and which reflect management’s best estimate of what market participants would use in pricing the asset or liability at the measurement date.

See Note 7, “Fair Value Measurements” for additional details.

Concentrations of Credit Risk

Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash and cash equivalents, accounts receivable, contract assets, equity securities, and restricted cash. Cash that is not required for immediate operating needs is invested principally in money market funds. Cash and cash equivalents are invested through banks and other financial institutions in the United States, India, and the Netherlands. Such deposits in those countries may be in excess of insured limits.

Accounts Receivable and Allowance for Doubtful Accounts

We currently sell primarily to pharmaceutical and fine chemicals companies throughout the world by the extension of trade credit terms based on an assessment of each customer's financial condition. Trade credit terms are generally offered without collateral and may include an insignificant discount for prompt payment for specific customers. To manage our credit exposure, we perform ongoing evaluations of our customers' financial conditions. In addition, accounts receivable includes amounts owed to us under our collaborative research and development agreements. We recognize accounts receivable at invoiced amounts and we maintain a valuation allowance for doubtful accounts.

The allowances for doubtful accounts reflect our best estimates of probable losses inherent in the accounts receivable and contract assets’ balances. We determine the allowances based on known troubled accounts, historical experience, and other currently available evidence. Uncollectible accounts receivables and contract assets are written off against the allowance for doubtful accounts when all efforts to collect them have been exhausted. Recoveries are recognized when they are received.

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Actual collection losses may differ from our estimates and could be material to our consolidated financial position, results of operations, and cash flows.

Unbilled receivable

Pursuant to ASC 606, the timing of revenue recognition may differ from the timing of invoicing to our customers. When we satisfy (or partially satisfy) a performance obligation, prior to being able to invoice the customer, we recognize an unbilled receivable when the right to consideration is unconditional. As of December 31, 2018, we recorded a total of unbilled receivables of $2.7 million included on our consolidated balance sheets.

Inventories

Inventories are stated at the lower of cost or net realizable value. Cost is determined using a weighted-average approach, assuming full absorption of direct and indirect manufacturing costs, or based on cost of purchasing from our vendors. If inventory costs exceed expected net realizable value due to obsolescence or lack of demand, valuation adjustments are recorded for the difference between the cost and the expected net realizable value.

Concentrations of Supply Risk

We rely on a limited number of suppliers for our products. We believe that other vendors would be able to provide similar products; however, the qualification of such vendors may require substantial start-up time. In order to mitigate any adverse impacts from a disruption of supply, we attempt to maintain an adequate supply of critical single-sourced materials. For certain materials, our vendors maintain a supply for us. We outsource the large scale manufacturing of our products to contract manufacturers with facilities in Austria and Italy.

Property and Equipment

Property, equipment and leasehold improvements are stated at cost less accumulated depreciation and amortization and depreciated using the straight-line method over their estimated useful lives as follows:

Asset classification	Estimated useful life
Laboratory equipment	5 years
Computer equipment and software	3 to 5 years
Office equipment and furniture	5 years
Leasehold improvements	Lesser of useful life or lease term

Property and equipment classified as construction in process includes equipment that has been received but not yet placed in service. Normal repairs and maintenance costs are expensed as incurred.

Impairment of Long-Lived Assets

Our tangible long-lived assets consist primarily of property and equipment.

In the first quarter of 2018, we determined that we operate in two segments. We have not identified property and equipment by segment since these assets are shared or commingled. We evaluate the carrying value of long-lived assets, including property and equipment, whenever events, changes in business circumstances or our planned use of long-lived assets indicate that their carrying amounts may not be fully recoverable or that their useful lives are no longer appropriate. If these facts and circumstances exist, we assess for recovery by comparing the carrying values of long-lived assets with their future net undiscounted cash flows. If the comparison indicates that impairment exists, long-lived assets are written down to their respective fair values based on discounted cash flows. Significant management judgment is required in the forecast of future operating results that are used in the preparation of unexpected undiscounted cash flows.

As of December 31, 2018 and 2017, there were no events or changes in circumstances which indicated that the carrying amount of our Asset Group might not be recoverable. No impairment charges for long-lived assets were recorded during the years ended December 31, 2018, 2017 and 2016.

Goodwill

Goodwill represents the excess of the consideration transferred over the fair value of net assets of businesses acquired and is assigned to reporting units. We test goodwill for impairment considering amongst other things, whether there have been

sustained declines in our share price. If we conclude it is more likely than not that the fair value of a reporting unit is less than its carrying amount, a quantitative fair value test is performed. In the first quarter of 2018, we determined that we operate in two segments and accordingly we re-evaluated our assessment of the number of reporting units. We concluded that we have two reporting units that reflect our operating segments and accordingly, we tested goodwill for impairment at the reporting unit level. Historically, assets are jointly used by the segments, are not separable, and are not identified by reporting unit. In order to assign the amount of goodwill to the two reporting units, we used a relative fair value allocation methodology that primarily relied on our estimates of revenue and future earnings for each reporting units. Using the relative fair value allocation methodology, we have determined that approximately 76% of goodwill is allocated to the Performance Enzymes segment and 24% is allocated to the Novel Biotherapeutics segment. As a result of the calculation, $2.4 million of the goodwill was assigned to the Performance Enzymes segment and $0.8 million was assigned to the Novel Biotherapeutics segment. There were no changes in the amount of goodwill assigned to each reporting unit at the end of the year.

The goodwill impairment test consists of a two-step process. The first step of the goodwill impairment test, used to identify potential impairment, compares the fair value of each reporting unit to its carrying value. Using the relative fair value allocation methodology, we compared the allocated carrying amount of each reporting unit's net assets and the assigned goodwill to its fair value. If the fair value of the reporting unit exceeds its carrying amount, goodwill of the reporting unit is considered not impaired, and the second step of the impairment test is not required. The second step, if required, compares the implied fair value of the reporting unit's goodwill with the carrying amount of that goodwill. Implied fair value is the excess of the fair value of the reporting unit over the fair value of all identified or allocated assets and liabilities. Any excess of the reporting unit's carrying amount goodwill over the respective implied fair value is recognized as an impairment. During 2018, 2017 and 2016, we did not record impairment charges related to goodwill.

We test goodwill for impairment on an annual basis on the last day of the fourth fiscal quarter and, when specific circumstances dictate, between annual tests by first assessing qualitative factors to determine whether it is more likely than not that the fair value of a reporting unit is less than its carrying amount. During 2018, 2017 and 2016, we did not record impairment charges related to goodwill.

Income Taxes

We use the liability method of accounting for income taxes, whereby deferred tax asset or liability account balances are calculated at the balance sheet date using current tax laws and rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are provided when necessary to reduce deferred tax assets to the amount that will more likely than not be realized.

We make certain estimates and judgments in determining income tax expense for financial statement purposes. These estimates and judgments occur in the calculation of tax credits, benefits and deductions and in the calculation of certain tax assets and liabilities, which arise from differences in the timing of recognition of revenues and expenses for tax and financial statement purposes. Significant changes to these estimates may result in an increase or decrease to our tax provision in a subsequent period.

In assessing the realizability of deferred tax assets, we consider whether it is more likely than not that some portion or all of the deferred tax assets will be realized on a jurisdiction by jurisdiction basis. The ultimate realization of deferred tax assets is dependent upon the generation of taxable income in the future. We have recorded a valuation allowance against these deferred tax assets in jurisdictions where ultimate realization of deferred tax assets is more likely than not to occur. As of December 31, 2018, we maintain a full valuation allowance in all jurisdictions against the net deferred tax assets as we believe that it is more likely than not that the majority of deferred tax assets will not be realized.

We make estimates and judgments about our future taxable income that are based on assumptions that are consistent with our plans and estimates. Should the actual amounts differ from our estimates, the amount of our valuation allowance may be materially impacted. Any adjustment to the deferred tax asset valuation allowance would be recorded in the statements of operations for the periods in which the adjustment is determined to be required.

We account for uncertainty in income taxes as required by the provisions of ASU 2009-06, Income Taxes (Topic 740) "Implementation Guidance on Accounting for Uncertainty in Income Taxes and Disclosure Amendments for

Nonpublic Entities", which clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to estimate and measure the tax benefit as the largest amount that is more than 50% likely of being realized upon ultimate settlement. It is inherently difficult and subjective to estimate such amounts, as this requires us to

determine the probability of various possible outcomes. We consider many factors when evaluating and estimating our tax positions and tax benefits, which may require periodic adjustments and may not accurately anticipate actual outcomes.

The Tax Reform Act of 1986 and similar state provisions limit the use of net operating loss ("NOL") carryforwards in certain situations where equity transactions result in a change of ownership as defined by Internal Revenue Code Section 382. In the event we should experience such a change of ownership, utilization of our federal and state NOL carryforwards could be limited.

The adoption of ASC 606 primarily resulted in less revenue recognized as of January 1, 2018, which in turn generated an increase in net deferred tax assets. As we fully reserve our net deferred tax assets in the jurisdictions impacted by the adoption of ASC 606, this impact was offset by a corresponding increase to the valuation allowance.

We recognized income tax benefit of $37 thousand, income tax provision of $81 thousand and income tax benefit of $40 thousand for the years ended December 31, 2018, 2017 and 2016, respectively. The income tax benefits were due to a net loss from our foreign operation and a reduction in the deferred tax liability for accrued future withholding taxes on dividends. We continue to maintain a full valuation allowance against our net deferred tax assets as we believe that it is more likely than not that the majority of our deferred tax assets will not be realized.

Changes to Tax Law

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 (the "Tax Act") was signed into law making significant changes to the Internal Revenue Code. The Tax Act made broad and complex changes to the U.S. tax code, including, but not limited to, (i) reducing the U.S. federal statutory tax rate from 35% to 21%; (ii) requiring companies to pay a one-time transition tax on certain un-repatriated earnings of foreign subsidiaries; (iii) generally eliminating U.S federal income taxes on dividends from foreign subsidiaries; (iv) requiring a current inclusion in U.S. federal taxable income of certain earnings of controlled foreign corporations; (v) eliminating the corporate alternative minimum tax ("AMT") and changing how existing AMT credits can be realized; (vi) creating the base erosion anti-abuse tax ("BEAT"), a new minimum tax; (vii) creating a tax on global intangible low-taxed income ("GILTI") of foreign subsidiaries; (viii) creating a new limitation on deductible interest expense; (ix) changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017; and (x) modifying the officer's compensation limitation.

In December 2017, the SEC issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provided a measurement period of up to one year from the enactment date of the Tax Act for companies to complete the accounting for the Tax Act and its related impacts. In 2018, we completed our accounting for the Tax Act. The income tax effects of the Tax Act for which the accounting is now complete include: the impact of the transition tax, the revaluation of deferred tax assets and liabilities to reflect the 21% corporate tax rate, and the impact to the aforementioned items on state income taxes. We have completed our accounting for the income tax effects under the Tax Act that are relevant to us and required to be recorded and disclosed pursuant to FASB ASC 740, Income Taxes. Accordingly, any and all provisional amounts previously recorded in accordance with SEC Staff Accounting Bulletin No. 118 have been adjusted to reflect their final amounts.

Because ASC 740-10-25-47 requires the effect of a change in tax laws or rates to be recognized as of the date of enactment, we remeasured our deferred tax assets and liabilities, and offsetting valuation allowance in 2017. There was no impact to tax expense as the remeasurement of net deferred tax assets was completely offset by a corresponding change in valuation allowance. The reduction to U.S. deferred tax assets and the offsetting valuation allowance was $34.1 million.

Beginning in 2018, the GILTI provisions in the Tax Act require us to include, in our U.S. income tax return, foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. Per guidance issued by the FASB, companies can either account for deferred taxes related to GILTI or treat tax arising from GILTI as a period cost. Both are acceptable methods subject to an accounting policy election. At December 31, 2018, we

finalized our policy and have elected to use the period cost method for GILTI. In 2018, we did not incur any GILTI inclusion as our foreign subsidiaries generated losses.

The BEAT provisions in the Tax Act eliminate the deduction of certain base-erosion payments made to related foreign corporations, and impose a minimum base erosion anti-abuse tax if greater than regular tax. In 2018, our company was not subject to BEAT as it did not meet the requirements to be subject to BEAT.

Recent Accounting Pronouncements
Recently adopted accounting pronouncement

In May 2014, the FASB issued ASU 2014-09, "Revenue from Contracts with Customers (Topic 606)" , (“ASC 606”), amending revenue recognition guidance and requiring more detailed disclosures to enable users of financial statements to understand the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers is effective for annual and interim reporting periods beginning after December 15, 2017, with early adoption permitted for public companies effective for annual and interim reporting periods beginning after December 15, 2016. We have adopted the provisions of ASC 606 and the related amendments, effective January 1, 2018, using the modified retrospective transition method. We recognized the cumulative effect of applying the new revenue standard and recognized a $4.1 million increase to the opening balance of the accumulated deficit at the beginning of 2018. The comparative information has not been restated and continues to be reported under the accounting standards in effect for the period presented. See Note 3, "Revenue Recognition" for more details.

In January 2016, the FASB issued ASU No. 2016-01, "Financial Instruments-Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities" (“Subtopic 825-10”). This guidance principally affects accounting standards for equity investments, financial liabilities where the fair value option has been elected, and the presentation and disclosure requirements for financial instruments. Upon the effective date of this new guidance, all equity investments in unconsolidated entities, other than those accounted for using the equity method of accounting, will generally be measured at fair value through earnings. There will no longer be an available-for-sale classification and therefore no changes in fair value will be reported in other comprehensive income (loss) for equity securities with readily determinable fair values. This new guidance primarily impacts our accounting for equity investments. In February 2018, the FASB issued ASU 2018-03, "Technical Corrections and Improvements to Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities, that clarifies the guidance in ASU No. 2016-01, Financial Instruments—Overall (Subtopic 825-10)." Prior to the adoption of ASC 825, we recognized unrealized holding gains and losses from our equity investment in CO2 Solutions in other comprehensive loss. We adopted ASC 825 in the first quarter of 2018 using a modified retrospective approach by means of a cumulative-effect adjustment to accumulated deficit. Upon adoption of ASC 825, we reclassified $0.5 million of unrealized loss (net of $0.6 million tax) from other accumulated comprehensive loss to beginning accumulated deficit. Any changes in the fair value of our equity investments, except those accounted for under the equity method, will be recognized in earnings on a prospective basis.

In August 2016, the FASB issued ASU 2016-15, "Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments" (“ASC 230”), which provides the FASB's guidance on certain cash flow statements items. ASC 230 is effective for fiscal reporting periods beginning after December 15, 2017, including interim periods within those fiscal years. We adopted ASC 230 in the first quarter of 2018, and the adoption had no impact on our annual consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, "Statement of Cash Flows (Topic 230) Restricted Cash a consensus of the FASB Emerging Issues Task Force” (“ASC 230”). The standard requires restricted cash and restricted cash equivalents to be included with cash and cash equivalents on the statement of cash flows. We adopted ASU 2016-18 in the first quarter of 2018 and the adoption had no material impact on our annual consolidated financial statements. The effect of the adoption of ASC 230 on our consolidated statements of cash flows was to include restricted cash balances in the beginning and end of period balances of cash and cash equivalents and restricted cash. The change in restricted cash was previously disclosed in operating and investing activities in the consolidated statements of cash flows.

In January 2017, the FASB issued ASU No. 2017-01 "Business Combinations (Topic 805): Clarifying the Definition of a Business” (“ASC 805”). The guidance requires the use of a framework to determine whether a set of assets and

activities constitutes an acquired or a sold business. The guidance is effective for fiscal reporting periods beginning after December 15, 2017, including interim periods within those fiscal years. The amendments should be applied prospectively as of the beginning of the period of adoption. We adopted ASC 805 in the first quarter of 2018, and the adoption had no impact on our annual consolidated financial statements.

In May 2017, the FASB issued ASU No. 2017-09, "Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting" ("ASC 718"). The amendments provide guidance on determining which changes to the terms and conditions of share-based payment awards require an entity to apply modification accounting under Topic 718. The new standard is effective for annual periods, including interim periods within those annual periods, beginning after December 15, 2017 with early adoption permitted. We adopted ASC 718 in the first quarter of 2018 and the adoption had no impact on our annual consolidated financial statements.

In March 2018, the FASB issued ASU 2018-05, "Income Taxes (Topic 740): Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118" (“ASC 740”) which amends Topic 740 by incorporating the SEC Staff Accounting Bulletin No. 118 (SAB 118) issued on December 22, 2017. SAB 118 provides guidance on accounting for the effects of the Tax Cuts and Jobs Act (Tax Reform) and allows a company to record provisional amounts during a measurement period not to extend beyond one year from the enactment date. See Income Taxes section above for additional information.

Recently issued accounting pronouncements not yet adopted

From time to time, new accounting pronouncements are issued by the FASB or other standards setting bodies that are adopted by us as of the specified effective date. Unless otherwise discussed, we believe that the impact of recently issued standards that are not yet effective will not have a material impact on our consolidated financial statements upon adoption.

In February 2016, the FASB issued ASU 2016-02, "Leases (Topic 842)" (“ASC 842”), which replaces prior lease guidance (“ASC 840”). This guidance establishes a right-of-use ("ROU") model that requires a lessee to record a ROU asset and lease liability on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the Consolidated Statement of Operations. The guidance also eliminates today’s real estate-specific provisions for all entities. For lessors, the guidance modifies the classification criteria and the accounting for sales-type and direct financing leases. Entities are required to use a modified retrospective approach for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. Entities have the option to use certain practical expedients. Full retrospective application is prohibited. ASC 842 is effective for public business entities for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years. Early adoption is permitted. In July 2018, the FASB issued ASU 2018-10, "Codification Improvements to ASC 842, Leases." These amendments affect narrow aspects of the guidance issued in the amendments in ASU 2016-02 including those regarding residual value guarantees, rate implicit in the lease, lessee reassessment of lease classification, lessor reassessment of lease term and purchase option, variable lease payments that depend on an index or a rate, investment tax credits, lease term and purchase option, transition guidance for amounts previously recognized in business combinations, certain transition adjustments, transition guidance for leases previously classified as capital leases under ASC 840, transition guidance for modifications to leases previously classified as direct financing or sales-type leases under ASC 840, transition guidance for sale and leaseback transactions, impairment of net investment in the lease, unguaranteed residual asset, effect of initial direct costs on rate implicit in the lease, and failed sale and leaseback transactions. For entities that have not adopted ASC 842, the effective date and transition requirements will be the same as the effective date and transition requirements in ASC 842. The FASB also issued ASU 2018-11, "Leases (Topic 842): Targeted Improvements." These amendments provide entities with an additional (and optional) transition method to adopt the new leases standard. Under this new transition method, an entity initially applies the new leases standard at the adoption date and recognizes a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. Consequently, an entity’s reporting for the comparative periods presented in the financial statements in which it adopts the new leases standard will continue to be in accordance with current GAAP (Topic 840, Leases). The amendments also provide lessors with a practical expedient, by class of underlying asset, to not separate nonlease components from the associated lease component and, instead, to account for those components as a single component if the nonlease components otherwise would be accounted for under ASC 606 and certain criteria are met. If the nonlease component or components associated with the lease component are the predominant component of the combined component, an entity is required to account for the combined component in accordance with ASC 606. Otherwise, the entity must account for the combined component as an operating lease in accordance with ASC 842. For entities that have not adopted ASC 842 before the issuance of ASU No. 2018-11, the effective date and transition requirements for the amendments related to separating components of a contract are the same as the effective date and transition requirements in ASU No. 2016-02. We plan to adopt ASC 842 on January 1, 2019 using a modified retrospective approach and effective date method per adoption of ASU 2018-11. We will recognize and measure all leases within the scope of the standard that exist as of January 1, 2017, beginning of the earliest period, as

if the standard had always been applied, subject to the practical expedients and transition relief in “Practical Expedients” section. In the current period, we evaluated the practical expedients elections and on adoption, and may apply a practical expedient in which an entity need not reassess whether any expired or existing contracts are or contain leases; An entity need not reassess the lease classification for any expired or existing leases (for example, all existing leases that were classified as operating leases in accordance with ASC 840 will be classified as operating leases, and all existing leases that were classified as capital leases in accordance with ASC 840 will be classified as finance leases); An entity need not reassess initial direct costs for any existing leases. We started the transition plan in the third quarter of 2018 and continued to perform the scoping work in the fourth quarter of 2018. We identified a total of 13 lease agreements that are subject to ASC 842 and seven of them meet the short-term lease exception. We completed the full analysis by January, 2019 and we evaluated the right-of-use (ROU) assets and lease liability using the incremental borrowing rate (IBR) at December 31, 2018 because the implicit rate is not readily determinable in the lease agreement. Upon adoption of ASC 842, all existing leases will be classified as either operating lease or finance lease. We expect to record a range from $20 million to $30 million of ROU assets and liabilities for operating leases and a range from $0.1 million to $0.8 million of ROU assets and liabilities for finance leases in

the balance sheet during the first quarter of 2019. This analysis was inclusive of the eighth amendment to the lease agreement disclosed in Note 16, “Subsequent Events.”
In June 2016, the FASB issued ASU 2016-13, "Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments," which amends the FASB's guidance on the impairment of financial instruments. The standard adds a new impairment model (known as the "current expected credit loss model") that is based on expected losses rather than incurred losses. ASU 2016-13 is effective for annual reporting periods ending after December 15, 2019, including interim periods within those fiscal years. Early adoption is permitted for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. We are currently evaluating the impact of adopting ASU 2016-13 on our consolidated financial statements and related disclosures.
In January 2017, the FASB issued ASU No. 2017-04, "Intangibles - Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment." The amendments eliminate Step 2 from the goodwill impairment test. The annual, or interim, goodwill impairment test is performed by comparing the fair value of a reporting unit with its carrying amount. An impairment charge should be recognized for the amount by which the carrying amount exceeds the reporting unit’s fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to that reporting unit. In addition, income tax effects from any tax deductible goodwill on the carrying amount of the reporting unit should be considered when measuring the goodwill impairment loss, if applicable. The amendments also eliminate the requirements for any reporting unit with a zero or negative carrying amount to perform a qualitative assessment and, if it fails that qualitative test, to perform Step 2 of the goodwill impairment test. An entity still has the option to perform the qualitative assessment for a reporting unit to determine if the quantitative impairment test is necessary. The new standard is effective for fiscal years beginning after December 15, 2019, with early adoption permitted. We do not expect the adoption of this standard to have a material impact on our consolidated financial statements and related disclosures.

In February 2018, the FASB issued ASU No. 2018-02, “Income Statement - Reporting Comprehensive Income (Topic 220) - Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income”. This standard allows a reclassification from accumulated other comprehensive income to retained earnings for stranded tax effects resulting from the Tax Cuts and Jobs Act and requires certain disclosures about stranded tax effects and will be effective for us beginning January 1, 2019 and should be applied either in the period of adoption or retrospectively. Early adoption is permitted. We do not expect this standard to have any impact on our consolidated financial statements.

In June 2018, the FASB issued ASU 2018-07, "Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting," which expands the scope of Topic 718, Compensation—Stock Compensation (which currently only includes share-based payments to employees) to include share-based payments issued to nonemployees for goods or services. Consequently, the accounting for share-based payments to nonemployees and employees will be substantially aligned. The ASU supersedes Subtopic 505-50, Equity—Equity-Based Payments to Non-Employees. The new standard is effective for fiscal years beginning after December 15, 2018, with early adoption permitted. We do not expect the adoption of this standard to have a material impact on our consolidated financial statements and related disclosures.

In July 2018, the FASB issued ASU 2018-09, "Codification Improvements”, which represent changes to clarify, correct errors in, or make minor improvements to the Codification, eliminating inconsistencies and providing clarifications in current guidance. The amendments in this ASU include those made to: Subtopic 220-10, Income Statement-Reporting Comprehensive Income-Overall; Subtopic 470-50, Debt-Modifications and Extinguishments; Subtopic 480-10, Distinguishing Liabilities from Equity-Overall; Subtopic 718-740, Compensation-Stock Compensation-Income Taxes; Subtopic 805-740, Business Combinations-Income Taxes; Subtopic 815-10, Derivatives and Hedging-Overall; Subtopic 820-10, Fair Value Measurement-Overall; Subtopic 940-405, Financial Services-Brokers and Dealers-Liabilities; and Subtopic 962-325, Plan Accounting-Defined Contribution Pension Plans-Investments-Other. The transition and effective date guidance is based on the facts and circumstances of each amendment. Some of the amendments do not require transition guidance and will be effective upon issuance. However, many of the

amendments do have transition guidance with effective dates for annual periods beginning after December 15, 2018, for public business entities. We do not expect this standard to have any material impact on our consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, "Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement." The primary focus of ASU 2018-13 is to improve the effectiveness of the disclosure requirements for fair value measurements. The changes affect all companies that are required to include fair value measurement disclosures. In general, the amendments in this standard are effective for all entities for fiscal years and interim periods within those fiscal years, beginning after December 15, 2019. Early adoption is permitted. We do not expect this standard to have any material impact on our consolidated financial statements.

In November 2018, the FASB issued ASU 2018-18, "Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606." ASU 2018-18 provides guidance on how to assess whether certain transactions between collaborative arrangement participants should be accounted for within the revenue recognition standard. The ASU also provides more comparability in the presentation of revenue for certain transactions between collaborative arrangement participants. In general, for public companies, the amendments in this standard are effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted. We do not expect this standard to have any material impact on our consolidated financial statements.

In November 2018, the FASB issued ASU 2018-19, "Codification Improvements to Topic 326, Financial Instruments—Credit Losses." ASU 2018-19 clarifies that receivables arising from operating leases are not within the scope of the credit losses standard, but rather, should be accounted for in accordance with the leases standard. In general, the amendments in this standard are effective for public business entities that meet the definition of a SEC filer for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. We do not expect this standard to have any material impact on our consolidated financial statements.

Note 3. Revenue Recognition

On January 1, 2018, we adopted ASC 606, applying the modified retrospective method to all contracts that were not completed as of that date. Results for reporting periods beginning after January 1, 2018 are presented under ASC 606 while prior period results are not adjusted and continue to be reported under the accounting standards in effect for the prior period. We recorded an increase to opening accumulated deficit of $4.1 million as of January 1, 2018 due to the cumulative impact of adopting ASC 606. The impact on revenue for the year ended December 31, 2018 was an increase of $5.0 million as a result of adopting ASC 606. The increase in revenues from the adoption of ASC 606 was primarily due to revenue from a product that was recognized over time as we have a right to payment from the customer under a binding, non-cancellable purchase order, and there is no alternate use of the product for us as it is specifically for the customer’s use, and revenues from research and development contracts that were recognized when we had the right to invoice our customers for monthly services completed to date. Also, revenue from a distinct, functional license granted on January 1, 2018 contributed to the increase in revenue from the adoption of ASC 606.

We are entitled to certain future milestone payments under our collaborative arrangements. Such milestone payments represent variable consideration that was fully constrained as the realization of the variable consideration is highly uncertain.

Disaggregation of Revenue

The following table provides information about disaggregated revenue from contracts with customers into the nature of the products and services, and geographic regions, and includes a reconciliation of the disaggregated revenue with reportable segments. The geographic regions that are tracked are the Americas (United States, Canada, Latin America), EMEA (Europe, Middle East, Africa), and APAC (Australia, New Zealand, Southeast Asia, China).

We identified our biotherapeutics business as a standalone business segment in the beginning of 2018 and revenues related to the Novel Biotherapeutics segment were first generated in 2017. Therefore, segment information for fiscal year 2016 is not provided.

Segment information for fiscal year 2018 is as follows (in thousands):

	Year Ended December 31, 2018		
	Performance Enzymes	Novel Biotherapeutics	Total
Major products and service:			
Product Revenue	$25,590	$ —	$25,590
Research and development revenue	21,483	13,521	35,004
Total revenues	$47,073	$ 13,521	$60,594
Primary geographical markets:			
Americas	$15,332	$ 38	$15,370
EMEA	8,878	13,483	22,361
APAC	22,863	—	22,863
Total revenues	$47,073	$ 13,521	$60,594

Segment information for fiscal year 2017 is as follows (in thousands):

	Year Ended December 31, 2017		
	Performance Enzymes	Novel Biotherapeutics	Total
Major products and service:			
Product Revenue	$26,685	$ —	$26,685
Research and development revenue	15,648	7,691	23,339
Total revenues	$42,333	$ 7,691	$50,024
Primary geographical markets:			
Americas	$15,575	$ —	$15,575
EMEA	11,919	7,691	19,610
APAC	14,839	—	14,839
Total revenues	$42,333	$ 7,691	$50,024

The following table shows the reconciliation of contract liabilities from what was disclosed in the Form 10-K for the year ended December 31, 2017 and gives effect to the modified retrospective adoption of the revenue guidance on January 1, 2018 (in thousands):

	Balance
Deferred Revenue, balance at December 31, 2017	$13,793
Changes in estimated consideration	—
Unsatisfied performance obligations	$5,173
Deferred Revenue, balance at January 1, 2018	$18,966

Contract Balances

The following table presents changes in the contract assets, unbilled receivable, contract costs, and contract liabilities (in thousands):

	January 1, 2018 balance	Additions	Deductions [1]	December 31, 2018
Contract Assets	$—	8,934	(8,899)	$ 35
Unbilled receivables, current	$—	2,908	(992)	$ 1,916
Unbilled receivables, non-current	$—	786	—	$ 786
Contract Costs	$239	—	(197)	$ 42
Contract Liabilities: Deferred Revenue	$18,966	6,446	(17,124)	$ 8,288

[1] The asset or liability balances are presented as a net position per contract and accordingly the deductions column includes the netting effect of presenting each contract on a net position basis as either a net liability or asset.

We recognize accounts receivable when we have an unconditional right to recognize revenue and have issued an invoice to the customer. Our payment terms are generally between 30 and 90 days. We recognize unbilled receivables when we have an unconditional right to recognize revenue and have not issued an invoice to our customer. Unbilled receivables, current are transferred to accounts receivable on issuance of an invoice. Unbilled receivables, non-current are transferred to accounts receivable on issuance of an invoice; payment is expected from the customer thereon. Unbilled receivables are classified separately on the consolidated balance sheet as assets.

Contract assets represent our right to recognize revenue for custom products with no alternate use and under binding non-cancellable purchase orders and are largely related to our procurement of product. We recognize contract assets when we have a conditional right to recognize revenue. The delivery pattern of certain of products occurs in advance of the invoicing process, which generates contract assets. In addition, we recognize a contract asset related to milestones not eligible for royalty accounting when we assess it is probable of being achieved and there will be no significant reversal of cumulative revenues. Contract assets are classified separately on the consolidated balance sheet as an asset and transferred to accounts receivable when our rights to payment become unconditional.

Contract liabilities, or deferred revenue, represent our obligation to transfer a product or service to the customer, and for which we have received consideration from the customer. We recognize a contract liability when we receive advance customer payments under development agreements for research and development services, upfront license payments, and from upfront customer payments received under product supply agreements. Contract liabilities are classified as a liability on the consolidated balance sheet.

Contract costs relate to incremental costs of obtaining a contract with a customer. Contract costs are amortized along with the associated revenue over the term of the contract.

We had no asset impairment charges related to contract assets in the period.

During the year ended December 31, 2018, we recognized the following revenues (in thousands):

Revenue recognized in the period for:	Year Ended December 31, 2018
Amounts included in contract liabilities at the beginning of the period:	
Performance obligations satisfied	$ 13,615
Changes in the period:	
Changes in the estimated transaction price allocated to performance obligations satisfied in prior periods	374
Performance obligations satisfied from new activities in the period - contract revenue	46,605
Total revenue	$ 60,594

Performance Obligations

The following table includes estimated revenue expected to be recognized in the future related to performance obligations that are unsatisfied or partially unsatisfied at the end of the reporting period. The estimated revenue does not include contracts with original durations of one year or less, amounts of variable consideration attributable to royalties, or contract renewals that are unexercised as of December 31, 2018. We did not recognize any revenue from performance obligations satisfied in previous periods.

The balances in the table below are partially based on judgments involved in estimating future orders from customers subject to the exercise of material rights pursuant to respective contracts (in thousands):

	2019	2020	2021	2022 and Thereafter	Total
Product Revenue	$2,201	$1,729	$1,623	$ —	$5,553
Research and development revenue	2,735	—	—	—	2,735
Total revenues	$4,936	$1,729	$1,623	$ —	$8,288

Practical Expedients, Elections, and Exemptions

We used a practical expedient available under ASC 606 which permits us to consider the aggregate effect of all contract modifications that occurred before the beginning of the earliest period presented when identifying satisfied and unsatisfied performance obligations, transaction price, and allocating the transaction price to the satisfied and unsatisfied performance obligations.

We also used a practical expedient available under ASC 606 which permits us not to adjust the amount of consideration for the effects of a significant financing component if, at contract inception, the expected period between the transfer of promised goods or services and customer payment is one year or less.

We perform monthly services under our research and development agreements and we use a practical expedient available under ASC 606 permitting us to recognize revenue at the same time that we have the right to invoice our customer for monthly services completed to date.

We have elected to treat shipping and handling activities as fulfillment costs.

Additionally, we have elected to record revenue net of sales and other similar taxes.

Impact on Financial Statements

In accordance with ASC 606, the disclosure of the impact of adoption to our consolidated statements of operations and balance sheets was as follows (in thousands, except per share amounts):

	Year Ended December 31, 2018		
	As reported	Adjustments	Balances without adoption of ASC 606
Revenues:			
Product revenue	$25,590	$ (3,422)	$22,168
Research and development revenue	35,004	(1,609)	33,395
Total revenues	60,594	(5,031)	55,563
Costs and operating expenses:			
Cost of product revenue	12,620	(285)	12,335
Research and development	29,978	(196)	29,782
Selling, general and administrative	29,291	—	29,291
Total costs and operating expenses	71,889	(481)	71,408
Loss from operations	(11,295)	(4,550)	(15,845)
Interest income	671	—	671
Other expenses	(291)	—	(291)
Loss before income taxes	(10,915)	(4,550)	(15,465)
Provision for (benefit from) income taxes	(37)	—	(37)
Net loss	$(10,878)	$ (4,550)	$(15,428)
Net loss per share, basic and diluted	$(0.21)	$ (0.09)	$(0.30)
Weighted average common shares used in computing net loss per share, basic and diluted	52,205		52,205

	December 31, 2018		
	As reported	Adjustments	Balances without adoption of ASC 606
Assets			
Accounts receivable	$11,551	$ (1,253)	$10,298
Unbilled receivables, current	1,916	(1,916)	—
Contract assets	35	(35)	—
Inventories	589	1	590
Unbilled receivables, non-current	786	(786)	—
Other non-current assets	265	(42)	223
Liabilities			
Other accrued liabilities	4,855	(520)	4,335
Deferred revenue - current	4,936	(1,574)	3,362
Deferred revenue - non-current	3,352	(1,445)	1,907
Stockholders' equity			
Accumulated deficit	(330,474)	(492)	(330,966)

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Note 4. Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of shares of common stock outstanding, less RSAs subject to forfeiture. Diluted net loss per share is computed by dividing net loss by the weighted-average number of shares of common stock outstanding, less RSAs subject to forfeiture, plus all additional common shares that would have been outstanding, assuming dilutive potential common shares had been issued for other dilutive securities. For all periods presented, diluted and basic net losses per share are identical since potential common shares are excluded from the calculation, as their effect was anti-dilutive.

Anti-Dilutive Securities

In periods of net loss, the weighted average number of shares outstanding related to potentially dilutive securities, prior to the application of the treasury stock method, are excluded from the computation of diluted net loss per common share because including such shares would have an anti-dilutive effect.

The following shares were not included in the computation of diluted net loss per share (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Shares issuable under Equity Incentive Plan	6,339	6,882	5,567
Shares issuable upon the conversion of warrants	—	—	73
Total anti-dilutive securities	6,339	6,882	5,640

Note 5. Collaborative Arrangements

Deferred revenue amounts discussed herein as of December 31, 2017 are derived from our Form 10-K for the year ended December 31, 2017. On January 1, 2018 we adopted Topic 606 and subsequently adjusted deferred revenue to give effect to the modified retrospective adoption of the revenue guidance. See Note 3, “Revenue Recognition” for additional information.

GSK Platform Technology Transfer, Collaboration and License Agreement

In July 2014, we entered into a CodeEvolver® protein engineering platform technology transfer collaboration and license agreement (the "GSK CodeEvolver® Agreement") with GlaxoSmithKline ("GSK"). Pursuant to the terms of the agreement, we granted GSK a non-exclusive license to use the CodeEvolver® protein engineering platform technology to develop novel enzymes for use in the manufacture of GSK's pharmaceutical and health care products. We received an upfront fee upon the execution of the agreement in July 2014 and milestone payments in each of the years from 2014 through April 2016. We completed the transfer of the CodeEvolver® protein engineering platform technology to GSK in April 2016 and all revenues relating to the technology transfer have been recognized as of April 2016. We have the potential to receive additional cumulative contingent payments that range from $5.75 million to $38.5 million per project based on GSK’s successful application of the licensed technology. We are also eligible to receive royalties based on net sales of GSK’s sales of licensed enzyme products that are currently not being recognized.

Merck Platform Technology Transfer and License Agreement

In August 2015, we entered into a CodeEvolver® platform technology transfer collaboration and license agreement (the "Merck CodeEvolver® Agreement") with Merck, Sharp & Dohme ("Merck") which allows Merck to use the CodeEvolver® protein engineering technology platform in the field of human and animal healthcare.

We received a $5.0 million up-front license fee upon execution of the Merck CodeEvolver® Agreement, and milestone payments in September 2015 and in September 2016, when we completed the transfer of the engineering platform technology. We recognized research and development revenues of $4.1 million, $3.6 million, and $3.0 million in 2018, 2017 and 2016, respectively, for various research projects under our collaborative arrangement.

We have the potential to receive payments of up to a maximum of $15.0 million for each commercial active pharmaceutical ingredient ("API") that is manufactured by Merck using one or more novel enzymes developed by Merck using the CodeEvolver® protein engineering technology platform. The API payments, which are currently not recognized in revenue, are based on quantity of API developed and manufactured by Merck and will be recognized as usage-based royalties.

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In October 2018, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we amended certain licensing provisions and one exhibit. In January 2019, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we will install certain CodeEvolver® protein engineering technology upgrades into Merck's platform license installation and maintain those upgrades for a multi-year term.

Merck Sitagliptin Catalyst Supply Agreement

In February 2012, we entered into a five-year Sitagliptin Catalyst Supply Agreement ("Sitagliptin Catalyst Supply Agreement") with Merck whereby Merck may obtain commercial scale enzyme for use in the manufacture of Januvia®, its product based on the active ingredient Sitagliptin. In December 2015, Merck exercised its option under the terms of the Sitagliptin Catalyst Supply Agreement to extend the agreement for an additional five years through February 2022. Effective as of January 2016, we and Merck amended the Sitagliptin Catalyst Supply Agreement to prospectively provide for variable pricing based on the cumulative volume of sitagliptin catalyst purchased by Merck and to allow Merck to purchase a percentage of its requirements for sitagliptin catalyst from a specified third-party supplier. Merck received a distinct, functional license to manufacture a portion of its demand beginning January 1, 2018, which we recognized as research and development revenue. We recognized research and development revenues of $1.3 million, $1.3 million and $1.3 million in 2018, 2017 and 2016, respectively.

In June 2017, we completed a contractual milestone by qualifying the specified third-party enzyme supplier and recognized $0.3 million as research and development revenues.

We have determined that the variable pricing, which provides a discount based on the cumulative volume of sitagliptin catalyst purchased by Merck, provides Merck material rights and we are recognizing product revenues using the alternative method. Under the alternative approach, we estimate the total expected consideration and allocate it proportionately with the expected sales.

The Sitagliptin Catalyst Supply Agreement requires Merck to pay an annual fee for the rights to the sitagliptin technology each year for the term of the Sitagliptin Catalyst Supply Agreement. Amounts of annual license fees are based on contractually agreed prices and are on a declining scale over the term of the contract.

We had a deferred revenue balance from Merck of $3.6 million at December 31, 2018 and $1.5 million at December 31, 2017. Pursuant to the terms of the Sitagliptin Catalyst Supply Agreement, Merck may purchase supply from us for a fee based on contractually stated prices and we recognized $12.3 million, $9.0 million and $5.9 million in 2018, 2017 and 2016, respectively, in product revenue under this agreement.

Enzyme Supply Agreement

In November 2016, we entered into a supply agreement whereby our customer may purchase quantities of one of our proprietary enzymes for use in its commercial manufacture of a product. Pursuant to the supply agreement, we received an upfront payment of $0.8 million in December 2016, which we accordingly recorded as deferred revenues. Such upfront payment will be recognized over the period of the supply agreement as the customer purchases our proprietary enzyme. We additionally have determined that the volume discounts under the supply agreement provides the customer material rights and we are recognizing revenues using the alternative method. As of December 31, 2018 and 2017, we had deferred revenue from the supply agreement of $2.0 million and $0.7 million, respectively.

Research and Development Agreement

In March 2017, we entered into a multi-year research and development services agreement with Tate & Lyle Ingredients Americas LLC ("Tate & Lyle") to develop enzymes for use in the manufacture of Tate & Lyle's zero-calorie TASTEVA® M Stevia sweetener. Under the agreement, we received an upfront payment of $3.0 million, which was originally recognized ratably over the maximum term of the services period of 21 months. Beginning January 1, 2018, we are recognizing revenue using a single measure of progress that depicts our performance in transferring the services. During the second quarter of 2018, Tate & Lyle opted to obtain additional development services that we completed by June 30, 2018 and we earned milestone payments upon completion of the services. We recognized $7.1 million and $3.2 million of revenue in 2018 and 2017, respectively, for research and development services under the research and development agreement. As of December 31, 2018 and 2017, we had deferred revenue from the development services agreement of zero and $3.1 million, respectively.

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Global Development, Option and License Agreement and Strategic Collaboration Agreement

In October 2017, we entered into a Global Development, Option and License Agreement (the "Nestlé Agreement") with Nestec Ltd. ("Nestlé Health Science") and, solely for the purpose of the integration and the dispute resolution clauses of the Nestlé Agreement, Nestlé Health Science S.A., to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU.

We received an upfront cash payment of $14.0 million in 2017 upon the execution of the Nestlé Agreement and a $4.0 million milestone payment 60 days after dosing the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114 for the potential treatment of PKU. The $4.0 million milestone payment that was triggered by the initiation of the trial was received in September 2018. The upfront payment and the variable consideration relating to the progress payment of $4.0 million are being recognized over time as the development work is being performed. Revenue is being recognized using a single measure of progress that depicts our performance in transferring control of the services, which is based on the ratio of level of effort incurred to date compared to the total estimated level of effort required to complete all performance obligations under the agreement. We recognized development fees of $9.9 million in 2018 as research and development revenue and $7.2 million in 2017. We had deferred revenue related to the development fees attributed to the milestone payment and up-front fees of $1.9 million at December 31, 2018 and $6.8 million at December 31, 2017.

In December 2018, Nestlé Health Science became obligated to pay us an additional $1.0 million within 60 days after the achievement of a milestone relating to formulation of CDX-6114. In January 2019, we received notice from the U.S. Food and Drug Administration (the “FDA”) that it had completed its review of our investigational new drug application (“IND”) for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, Nestlé Health Science is obligated to pay us $3.0 million within 60 days after exercise of the option. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, “Subsequent Events” in the notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details. Other potential payments from Nestlé Health Science to us under the Nestlé Agreement include (i) development and approval milestones of up to $86.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of Product.

In addition to the Nestlé Agreement, we and Nestlé Health Science concurrently entered into a Strategic Collaboration Agreement (the “Strategic Collaboration Agreement”) pursuant to which we and Nestlé Health Science will collaborate to leverage the CodeEvolver® protein engineering technology platform to develop novel enzymes for Nestlé Health Science’s established Consumer Care and Medical Nutrition business areas. Under the Strategic Collaboration Agreement, we received an upfront payment of $1.2 million in 2017 and an incremental $0.6 million payment in September 2018 for additional services. We recognized research and development fees of $3.6 million and $0.5 million in 2018 and 2017, respectively. As of December 31, 2018 and 2017, we had deferred revenue of $0.8 million and $1.1 million, respectively.

Strategic Collaboration Agreement

In April 2018, we entered into the Porton Agreement with Porton to license key elements of Codexis’ biocatalyst technology for use in Porton’s global custom intermediate and API development and manufacturing business. Under the Porton Agreement, we are eligible to receive annual collaboration fees and research and development revenues. We have the potential to receive performance payments based on products produced by Porton using our company technology under the license agreement. We received an initial collaboration fee of $0.5 million within 30 days of the effective date of the agreement. As of December 31, 2018, we completed the technical transfer and we recognized revenue of $2.8 million in 2018 as research and development revenue. Revenue relating to the functional license provided to Porton was recognized at a point in time when control of the license transferred to the customer.

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Note 6. Cash Equivalents and Equity Securities

Cash equivalents and equity securities at December 31, 2018 and 2017 consisted of the following (in thousands):

	December 31, 2018				
	Adjusted Cost	Gross Unrealized Gains [3]	Gross Unrealized Losses (3)	Estimated Fair Value	Average Contractual Maturities (in days)
Money market funds [1]	$31,225	$ —	$ —	$ 31,225	n/a
Common shares of CO_2 Solutions [2]	563	25	—	588	n/a
Total	$31,788	$ 25	$ —	$ 31,813	

	December 31, 2017				
	Adjusted Cost	Gross Unrealized Gains (3)	Gross Unrealized Losses (3)	Estimated Fair Value	Average Contractual Maturities (in days)
Money market funds [1]	$6,778	$ —	$ —	$ 6,778	n/a
Common shares of CO_2 Solutions [2]	563	108	—	671	n/a
Total	$7,341	$ 108	$ —	$ 7,449	

[1] Money market funds are classified in cash and cash equivalents on our consolidated balance sheets.

[2] Common shares of CO_2 Solutions are classified in equity securities on our consolidated balance sheets.

[3] As a result of adopting ASU 2016-01, in 2018 and thereafter gross unrealized gains and gross unrealized losses related to our investment in CO_2 Solutions were recognized in other expense, in the consolidated statements of operations. Prior to 2018 gross unrealized gains and gross unrealized losses related to our investment in CO_2 Solutions were recorded in accumulated other comprehensive loss on the balance sheet.

As of December 31, 2018, the total cash and cash equivalents balance of $53.0 million was comprised of money market funds of $31.2 million and cash of $21.8 million held with major financial institutions worldwide. As of December 31, 2017, the total cash and cash equivalents balance of $31.2 million was comprised of money market funds of $6.8 million and cash of $24.4 million held with major financial institutions worldwide.

In December 2009, we purchased 10,000,000 common shares of CO_2 Solutions, a company based in Quebec, Canada, whose shares are publicly traded in Canada on TSX Venture Exchange. Our purchase represented approximately 16.6% of CO_2 Solutions' total common shares outstanding at the time of investment and was made in a private placement subject to a four-month statutory resale restriction. This restriction expired on April 15, 2010. Our investment in CO_2 Solutions is recorded at its fair value. See Note 7, "Fair Value Measurements." Through December 31, 2018, we concluded that we did not have the ability to exercise significant influence over CO_2 Solutions' operating and financial policies.

On January 1, 2018, we adopted ASU 2016-01. Upon adoption, we reclassified the $0.5 million net unrealized loss from accumulated other comprehensive loss to our opening accumulated deficit.

In 2018, we recognized an unrealized loss of $84 thousand related to our investment in CO_2 Solutions in other expense, in the consolidated statements of operations.

Note 7. Fair Value Measurements

The following tables present the financial instruments that were measured at fair value on a recurring basis at December 31, 2018 and 2017 by level within the fair value hierarchy (in thousands):

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
Money market funds	$31,225	$ —	$ —	$31,225
Common shares of CO_2 Solutions	588	—	—	588
Total	$31,813	$ —	$ —	$31,813

	December 31, 2017			
	Level 1	Level 2	Level 3	Total
Money market funds	$6,778	$ —	$ —	$6,778
Common shares of CO_2 Solutions	—	671	—	671
Total	$6,778	$ 671	$ —	$7,449

We determine the fair value of Level 1 and Level 2 assets using quoted prices in active markets for identical assets. We estimated the fair value of our investment in 10,000,000 common shares of CO_2 Solutions using the market value of common shares as determined by trading on the TSX Venture Exchange, and we classified our investment in CO_2 Solutions within the fair value hierarchy as Level 1 and Level 2, at December 31, 2018 and December 31, 2017, respectively, using the quoted prices in an active market to determine their fair value.

A review of the fair value hierarchy classifications of our investments is conducted annually. Changes in the observability of valuation inputs may result in a reclassification for certain financial assets. Reclassifications are reported as transfers in or transfers out of the applicable level at end of the calendar year in which the reclassifications occur. In the fourth quarter of 2018, we reclassified the $0.6 million fair value of the investment in the common shares of CO_2 Solutions from Level 2 to Level 1 within the fair value hierarchy since we concluded that there was a sufficient level of transactional frequency and trading volume to indicate that the pricing information was representative of its fair value on an ongoing basis. (See also Note 6, “Cash Equivalents and Equity Securities” for additional information.)

Note 8. Balance Sheets Details

Accounts receivable

The following is a summary of activity in our allowance for doubtful accounts for the periods presented (in thousands):

	December 31,		
	2018	2017	2016
Allowance - beginning of period	$(34)	$(421)	$(421)
Write-offs and other [1]	—	387	—
Allowance - end of period	$(34)	$(34)	$(421)

[1] The change in allowance for doubtful accounts was mainly related to the write-off of receivables from a foreign customer.

Inventories

Inventories consisted of the following (in thousands):

	December 31,	
	2018	2017
Raw materials	$165	$158
Work in process	47	53
Finished goods	377	825
Inventories	$589	$1,036

Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2018	2017
Laboratory equipment [1]	$21,328	$19,777
Leasehold improvements	10,359	10,327
Computer equipment and software	3,954	3,695
Office equipment and furniture	1,272	1,185
Construction in progress [2]	939	85
Property and equipment	37,852	35,069
Less: accumulated depreciation and amortization	(33,093)	(32,254)
Property and equipment, net	$4,759	$2,815

[1] Fully depreciated laboratory equipment with a cost of $0.3 million and $0.2 million were retired during 2018 and 2017, respectively.

[2] Construction in progress includes equipment received but not yet placed into service pending installation.

Goodwill

Goodwill had a carrying value of approximately of $3.2 million as of December 31, 2018 and 2017.

Other Accrued Liabilities

Other accrued liabilities consisted of the following (in thousands):

	December 31,	
	2018	2017
Accrued purchases	$1,492	$941
Accrued professional and outside service fees	2,020	2,393
Deferred rent	343	258
Lease incentive obligation	425	425
Other	575	345
Total	$4,855	$4,362

Note 9. Stock-based Compensation

Equity Incentive Plans

In March 2010, our board of directors (the "Board") and stockholders approved the 2010 Equity Incentive Award Plan (the "2010 Plan"), which became effective upon the completion of our initial public offering in April 2010. The number of shares of our common stock available for issuance under the 2010 Plan is equal to 1,100,000 shares plus any shares of common stock reserved for future grant or issuance under our 2002 Stock Plan (the “2002 Plan”) that remained unissued at the time of completion of the initial public offering. The 2010 Plan also provides for automatic annual increases in the number of shares reserved for future issuance. All grants will reduce the 2010 Plan reserve by one share for every share granted. As of December 31, 2018, total shares remaining available for issuance under the 2010 Plan were approximately 7.9 million shares.

The 2010 Plan provides for the grant of incentive stock options, non-statutory stock options, RSUs, RSAs, PSUs, PBOs, stock appreciation rights, and stock purchase rights to our employees, non-employee directors and consultants.

Stock Options

The option exercise price for incentive stock options must be at least 100% of the fair value of our common stock on the date of grant and the option exercise price for non-statutory stock options is 85% of the fair value of our common stock on the date of grant, as determined by the Board. If, at the time of a grant, the optionee directly or by attribution owns stock possessing more than 10% of the total combined voting power of all of our outstanding capital stock, the exercise price for these options must be at least 110% of the fair value of the underlying common stock. Stock options granted to employees generally have a maximum term of 10 years and vest over 4 years from the date of grant, of which 25% vest at the end of one year, and 75% vest monthly over the remaining three years. We may grant options with different vesting terms from time to time. Unless an employee's termination of service is due to disability or death, upon termination of service, any unexercised vested options will be forfeited at the end of three months or the expiration of the option, whichever is earlier.

Restricted Stock Units (RSUs)

We also grant employees RSUs, which generally vest over either a three year period with one-third of the shares subject to the RSUs vesting on each yearly anniversary of the vesting commencement date or over a four year period with 25% of the shares subject to the RSU vesting on each yearly anniversary of the vesting commencement date, in each case contingent upon such employee’s continued service on such vesting date. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. We may grant RSUs with different vesting terms from time to time.

Performance-contingent Restricted Stock Units (PSUs) and Performance Based Options (PBOs)

The compensation committee of the Board approved, solely in respect of non-executive employees, delegated to our Chief Executive Officer the authority to approve grants of PSUs. The compensation committee of the Board also approved grants of PBOs and PSUs to our executives. The PSUs and PBOs vest based upon both the successful achievement of certain corporate operating milestones in specified timelines and continued employment through the applicable vesting date. When the performance goals are deemed to be probable of achievement for these types of awards, recognition of stock-based compensation expense commences. Once the number of shares eligible to vest is determined, those shares vest in two equal installments with 50% vesting upon achievement and the remaining 50%

vesting on the first anniversary of achievement, in each case, subject to the recipient's continued service through the applicable vesting date. If the performance goals are achieved at the threshold level, the number of shares eligible to vest in respect of the PSUs and PBOs would be equal to half the number

of PSUs granted and one-quarter the number of shares underlying the PBOs granted. If the performance goals are achieved at the target level, the number of shares eligible to vest in respect of the PSUs and PBOs would be equal to the number of PSUs granted and half of the shares underlying the PBOs granted. If the performance goals are achieved at the superior level, the number of shares eligible to vest in respect of the PSUs would be equal to two times the number of PSUs granted and equal to the number of PBOs granted. The number of shares issuable upon achievement of the performance goals at the levels between the threshold and target levels for the PSUs and PBOs or between the target level and superior levels for the PSUs would be determined using linear interpolation. Achievement below the threshold level would result in no shares being eligible to vest in respect of the PSUs and PBOs.

In the first quarter of 2018, we awarded PSUs ("2018 PSUs") and PBOs ("2018 PBOs"), each of which commence vesting based upon the achievement of various weighted performance goals, including core business revenue growth, cash balance, new licensing collaborations, new research and development service revenue arrangements, technology advancement and novel therapeutic enzymes advancement. As of December 31, 2018, we estimated that the 2018 PSUs and 2018 PBOs performance goals would be achieved at 118% of the target level, and recognized expenses accordingly.

In 2017, we awarded PSUs ("2017 PSUs") and PBOs ("2017 PBOs"), each of which commence vesting based upon the achievement of various weighted performance goals, including revenue growth, fundraising, service revenue, new platform license revenue, and strategic advancement of biotherapeutics pipeline. In the first quarter of 2018, we determined that the 2017 PSU and PBO performance goals had been achieved at 134.2% of the target level, and recognized expenses accordingly. Accordingly, one-half of the shares underlying the 2017 PSUs and PBOs vested in the first quarter of 2018 and one-half of the shares underlying the 2017 PSUs and PBOs will vest in the first quarter of 2019, in each case subject to the recipient’s continued service on each vesting date.

In 2016, we awarded PSUs ("2016 PSUs") based upon the achievement of various weighted performance goals, including revenue growth, non-GAAP net income growth, new licensing collaborations, new research and development service revenue arrangements and novel therapeutic enzymes advancement. In the first quarter of 2017, we determined that the 2016 PSU performance goals had been achieved at 142.3% of the target level, and recognized expenses accordingly. Accordingly, one-half of the shares underlying the 2016 PSUs vested in the first quarter of each of 2017 and 2018, in each case subject to the recipient’s continued service on each vesting date. No PBOs were awarded in 2016.

Stock-Based Compensation Expense:

Stock-based compensation expense is included in the consolidated statements of operations as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Research and development	$2,055	$1,444	$1,033
Selling, general and administrative	5,834	5,647	4,640
Total	$7,889	$7,091	$5,673

The following table presents total stock-based compensation expense by security type included in the consolidated statements of operations (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Stock options	$1,975	$1,554	$1,102
RSUs and RSAs	1,770	1,888	2,043
PSUs	1,511	1,792	2,528
PBOs	2,633	1,857	—
Total	$7,889	$7,091	$5,673

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Grant Award Activities:

Stock Option Awards

We estimated the fair value of stock options using the Black-Scholes-Merton option-pricing model based on the date of grant. The following summarize the ranges of weighted-average assumptions used to estimate the fair value of employee stock options granted:

	Year Ended December 31,		
	2018	2017	2016
Expected life (years)	5.6	5.4	5.3
Volatility	60.0 %	62.2 %	64.2 %
Risk-free interest rate	2.7 %	2.0 %	1.3 %
Expected dividend yield	0.0 %	0.0 %	0.0 %

In October 2017, we granted an option to purchase 11,100 shares of common stock to a non-employee as compensation for services valued at $48 thousand with the following assumptions used to estimate the fair value of non-employee stock options: (i) volatility rate at 60.6%, risk-free interest rate of 2.4% and (ii) no expected dividend yield. The option vested over a period of six months with one-sixth of total number of shares subject to the option vesting on each one month anniversary of the grant date. During the year ended December 31, 2018 and December 31, 2016, we did not grant any options to purchase shares of common stock to non-employees.

The following tables summarizes stock option activities:

	Number of Shares	Weighted Average Exercise Price Per Share
	(In Thousands)	
Outstanding at December 31, 2015	3,918	$ 4.49
Granted	971	$ 4.16
Exercised	(398)	$ 2.60
Forfeited/Expired	(601)	$ 5.76
Outstanding at December 31, 2016	3,890	$ 4.40
Granted	856	$ 4.57
Exercised	(86)	$ 3.10
Forfeited/Expired	(81)	$ 7.72
Outstanding at December 31, 2017	4,579	$ 4.40
Granted	645	$ 9.56
Exercised	(772)	$ 5.56
Forfeited/Expired	(340)	$ 6.66
Outstanding at December 31, 2018	4,112	$ 4.81
Exercisable at December 31, 2018	2,876	$ 3.83
Vested and expected to vest at December 31, 2018	3,954	$ 4.69

	Number of Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(In Years)	

	(In Thousands)			(In Thousands)
Outstanding at December 31, 2018	4,112	$ 4.81	6.23	$ 48,927
Exercisable at December 31, 2018	2,876	$ 3.83	5.25	$ 37,005
Vested and expected to vest at December 31, 2018	3,954	$ 4.69	6.13	$ 47,503

The weighted average grant date fair value per share of stock options granted in 2018, 2017 and 2016 were $5.34, $2.51 and $2.32, respectively. The total intrinsic value of options exercised in 2018, 2017 and 2016 were $7.6 million, $0.2 million and $0.6 million, respectively.

As of December 31, 2018, there was $3.5 million of unrecognized stock-based compensation cost related to non-vested options, which we expect to recognize over a weighted average period of 2.5 years.

Restricted Stock Awards (RSAs)

The following table summarizes RSA activities:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
	(In Thousands)	
Non-vested balance at December 31, 2015	480	$ 3.29
Granted	185	$ 4.21
Vested	(435)	$ 3.40
Non-vested balance at December 31, 2016	230	$ 3.82
Granted	143	$ 4.75
Vested	(214)	$ 3.81
Non-vested balance at December 31, 2017	159	$ 4.68
Granted	47	$ 14.35
Vested	(151)	$ 4.71
Non-vested balance at December 31, 2018	55	$ 12.83

The weighted average grant date fair value per share of RSAs granted in 2018, 2017 and 2016 were $14.35, $4.75 and $4.21, respectively. The total fair value of RSAs vested in fiscal 2018, 2017 and 2016 were $2.1 million, $1.0 million and $1.8 million respectively.

As of December 31, 2018, there was $0.3 million of unrecognized stock-based compensation cost related to non-vested RSAs, which we expect to recognize over a weighted average period of 0.4 years.

Restricted Stock Units (RSUs)

The following table summarizes RSU activities:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
	(In Thousands)	
Non-vested balance at January 1, 2016	545	$ 3.15
Granted	330	$ 4.10
Vested	(243)	$ 3.11
Forfeited/Expired	(15)	$ 2.74
Non-vested balance at December 31, 2016	617	$ 3.69
Granted	275	$ 4.22
Vested	(302)	$ 3.40
Forfeited/Expired	(30)	$ 4.12
Non-vested balance at December 31, 2017	560	$ 4.08
Granted	86	$ 10.56
Vested	(290)	$ 4.09
Forfeited/Expired	(8)	$ 4.73
Non-vested balance at December 31, 2018	348	$ 5.66

The weighted average grant date fair value per share of RSUs granted in 2018, 2017 and 2016 were $10.56, $4.22 and $4.10, respectively. The total fair value of RSUs vested in fiscal 2018, 2017 and 2016 were $2.9 million, $1.3 million and $1.0 million respectively.

As of December 31, 2018, there was $1.0 million of unrecognized stock-based compensation cost related to non-vested RSUs, which we expect to recognize over a weighted average period of 1.1 years.

Performance-Contingent Restricted Stock Units (PSUs)

The following table summarizes PSU activities:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
	(In Thousands)	
Non-vested balance at January 1, 2016	989	$ 2.94
Granted	629	$ 4.10
Vested	(482)	$ 2.89
Forfeited/Expired	(305)	$ 2.82
Non-vested balance at January 1, 2017	831	$ 3.88
Granted	276	$ 4.25
Vested	(651)	$ 3.84
Forfeited/Expired	(27)	$ 3.65
Non-vested balance at January 1, 2018	429	$ 4.20

Granted	306	$ 6.71
Vested	(495)	$ 4.16
Non-vested balance at December 31, 2018	240	$ 7.48

The weighted average grant date fair value per share of PSUs granted in 2018, 2017 and 2016 were $6.71, $4.25 and $4.10, respectively. The total fair value of PSUs vested in fiscal 2018, 2017, and 2016 were $5.4 million, $2.7 million, and $1.8 million, respectively.

As of December 31, 2018, there was $0.6 million of unrecognized stock-based compensation cost related to non-vested PSUs, which we expect to recognize over a weighted average period of 0.5 years.

Performance Based Options (PBOs)

We estimated the fair value of PBO using the Black-Scholes-Merton option-pricing model based on the date of grant. The following summarize the ranges of weighted-average assumptions used to estimate the fair value of employee stock options granted:

	Year Ended December 31,		
	2018	2017	2016
Expected life (years)	5.63	5.33	—
Volatility	60.3 %	62.3 %	—
Risk-free interest rate	5.6 %	5.3 %	—
Expected dividend yield	0.0 %	0.0 %	—

The following table summarizes PBO activities in 2018:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
	(in thousands)	
Outstanding at December 31, 2016	—	$ —
Granted	1,720	$ 2.54
Outstanding at December 31, 2017	1,720	$ 2.54
Granted	1,200	$ 5.02
Exercised	(84)	$ 2.54
Forfeited	(1,254)	$ 3.73
Outstanding at December 31, 2018	1,582	$ 3.47

	Number of Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
	(In Thousands)		(In Years)	(In Thousands)
Exercisable at December 31, 2018	493	$ 4.60	5.60	$ 5,968
Vested and expected to vest at December 31, 2018	1,582	$ 6.24	5.44	$ 16,553

The total fair value of exercised PBOs was $0.2 million for 2018, zero for 2017 and zero for 2016. As of December 31, 2018, there was $1.2 million of unrecognized stock-based compensation cost related to non-vested PBOs, which we expect to recognize over a weighted average period of 0.9 years.

Note 10. Capital Stock

Public Offering

In April 2018, we completed an underwritten public offering of 4,312,500 shares of our common stock, including the exercise in full by the underwriters of their option to purchase 562,500 of our shares, at a public offering price of $9.25 per share. After deducting the underwriting discounts and commissions and estimated offering expenses, net

proceeds were approximately $37.3 million.

Note 11. 401(k) Plan

In January 2005, we implemented a 401(k) Plan covering certain employees. Currently, all of our United States based employees over the age of 18 are eligible to participate in the 401(k) Plan. Under the 401(k) Plan, eligible employees may elect to reduce their current compensation up to a certain annual limit and contribute these amounts to the 401(k) Plan. We may make matching or other contributions to the 401(k) Plan on behalf of eligible employees. We recorded employer matching contributions expense of $0.6 million, $0.6 million and $0.4 million in 2018, 2017, and 2016, respectively.

Note 12. Income Taxes

Our loss before provision for income taxes was as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
United States	$(10,653)	$(22,994)	$(8,174)
Foreign	(262)	79	(424)
Loss before provision for income taxes	$(10,915)	$(22,915)	$(8,598)

The tax provision (benefit from) for the years ended December 31, 2018, 2017 and 2016 consists primarily of taxes attributable to foreign operations. The components of the provision for income taxes are as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Current provision (benefit):			
Federal	$—	$—	$—
State	5	5	5
Foreign	(13)	64	(14)
Total current provision (benefit)	(8)	69	(9)
Deferred provision (benefit):			
Federal	—	—	—
State	—	—	—
Foreign	(29)	12	(31)
Total deferred provision (benefit)	(29)	12	(31)
Provision for (benefit from) income taxes	$(37)	$81	$(40)

Reconciliation of the provision for income taxes calculated at the statutory rate to our provision for (benefit from) income taxes is as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Tax benefit at federal statutory rate	$(2,292)	$(7,791)	$(2,924)
State taxes	222	48	127
Research and development credits	(499)	(399)	(161)
Foreign operations taxed at different rates	(17)	(2)	30
Stock-based compensation	(2,587)	(216)	327
Other nondeductible items	(3)	326	405
Executive compensation	838	73	255
Change in valuation allowance	4,301	(26,058)	1,901
Change in statutory tax rate	—	34,100	—
Provision for (benefit from) income taxes	$(37)	$81	$(40)

Deferred income taxes reflect the net tax effects of (a) temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, and (b) operating losses and tax credit carryforwards.

Significant components of our deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating losses	$60,455	$53,901
Credits	7,174	6,221
Deferred revenues	1,879	3,334
Stock-based compensation	2,967	2,872
Reserves and accruals	1,876	2,028
Depreciation	1,376	1,573
Intangible assets	2,557	3,172
Capital losses	576	576
Unrealized gain/loss	297	295
Other assets	83	78
Total deferred tax assets:	79,240	74,050
Deferred tax liabilities:		
Other	(64)	(115)
Total deferred tax liabilities:	(64)	(115)
Valuation allowance	(79,222)	(74,010)
Net deferred tax liabilities	$(46)	$(75)

ASC Topic 740 requires that the tax benefit of NOLs, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is “more likely than not.” Realization of the future tax benefits is dependent on our ability to generate sufficient taxable income within the carryforward period. Because of our history of operating losses, management believes that recognition of the deferred tax assets arising from the above-mentioned future tax benefits is currently not more likely than not to be realized and, accordingly, has provided a valuation allowance against our deferred tax assets. Accordingly, the net deferred tax assets in all our jurisdictions have been fully reserved by a valuation allowance. The change in valuation allowance differs from the amount included the rate reconciliation table due to the deferred tax impact of the adoption of ASC 606, which resulted in a $0.9 million adjustment to opening accumulated deficit before the offsetting change in valuation allowance. The net valuation allowance increased by $5.2 million during the year ended December 31, 2018; and decreased by $20.4 million during the year ended December 31, 2017; and increased by $1.9 million during the year ended December 31, 2016, respectively. At such time as it is determined that it is more likely than not that the deferred tax assets are realizable, the valuation allowance will be reduced.

The following table sets forth our federal, state and foreign NOL carryforwards and federal research and development tax credits as of December 31, 2018 (in thousands):

	December 31, 2018	
	Amount	Expiration Years
Net operating losses, federal	$254,208	2022-2038
Net operating losses, state	115,420	2018-2038
Tax credits, federal	7,430	2022-2038
Tax credits, state	9,121	Do not expire
Net operating losses, foreign	383	Various

Current U.S. federal and California tax laws include substantial restrictions on the utilization of NOLs and tax credit carryforwards in the event of an ownership change of a corporation. Accordingly, the Company's ability to utilize NOLs and tax

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credit carryforwards may be limited as a result of such ownership changes. We performed an analysis in 2018 and determined that there was not a limitation that would result in the expiration of carryforwards before they are utilized.
Income tax expense or benefit from continuing operations is generally determined without regard to other categories of earnings, such as discontinued operations and other comprehensive income. An exception is provided in ASC Topic 740 when there is aggregate income from categories other than continuing operations and a loss from continuing operations in the current year. In this case, the tax benefit allocated to continuing operations is the amount by which the loss from continuing operations reduces the tax expenses recorded with respect to the other categories of earnings, even when a valuation allowance has been established against the deferred tax assets. In instances where a valuation allowance is established against current year losses, income from other sources, including gain from available-for-sale securities recorded as a component of other comprehensive income, is considered when determining whether sufficient future taxable income exists to realize the deferred tax assets. For the year ended December 31, 2018, we did not record a tax expense in other comprehensive income related to available-for-sale securities.
In 2014, we determined that the undistributed earnings of our India subsidiary will be repatriated to the United States, and accordingly, we have provided a deferred tax liability totaling $0.1 million as of December 31, 2018, for local taxes that would be incurred upon repatriation. We have not provided for U.S. federal and state income taxes on all of the remaining non-U.S. subsidiaries' undistributed earnings as of December 31, 2018 as the remaining foreign jurisdictions are in an accumulative loss position.
We apply the provisions of ASC Topic 740 to account for uncertainty in income taxes. A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Rollforward Table (at Gross): As of December 31,		
	2018	2017	2016
Balance at beginning of year	$9,422	$8,566	$8,152
Additions based on tax positions related to current year	1,087	880	459
Reductions to tax provision of prior years	(529)	(24)	(45)
Balance at end of year	$9,980	$9,422	$8,566

We recognize interest and penalties as a component of our income tax expense. Total interest and penalties recognized in the consolidated statement of operations was $37 thousand, $31 thousand and $35 thousand, respectively, in 2018, 2017 and 2016. Total penalties and interest recognized in the balance sheet was $0.4 million and $0.3 million, respectively, in 2018 and 2017. The total unrecognized tax benefits that, if recognized currently, would impact our company's effective tax rate were $0.3 million and $0.4 million as of December 31, 2018 and 2017, respectively. We do not expect any material changes to our uncertain tax positions within the next 12 months. We are not subject to examination by United States federal or state tax authorities for years prior to 2002 and foreign tax authorities for years prior to 2012.
On December 22, 2017, the Tax Cuts and Jobs Act of 2017 (the "Act") was signed into law making significant changes to the Internal Revenue Code. The Act made broad and complex changes to the U.S. tax code, including, but not limited to, (i) reducing the U.S. federal statutory tax rate from 35% to 21%; (ii) requiring companies to pay a one-time transition tax on certain un-repatriated earnings of foreign subsidiaries; (iii) generally eliminating U.S federal income taxes on dividends from foreign subsidiaries; (iv) requiring a current inclusion in U.S. federal taxable income of certain earnings of controlled foreign corporations; (v) eliminating the corporate alternative minimum tax (AMT) and changing how existing AMT credits can be realized; (vi) creating the base erosion anti-abuse tax (BEAT), a new minimum tax; (vii) creating a tax on global intangible low-taxed income (GILTI) of foreign subsidiaries; (viii) creating a new limitation on deductible interest expense; (ix) changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017; and (x) modifying the officer's compensation limitation.

In December 2017, the SEC issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provided a measurement period of up to one year from the enactment date of the Tax Act for companies to complete the accounting for the Tax Act and its related impacts. In 2018, we completed our accounting for the Tax Act. The income tax effects of the Tax Act for which the accounting is now completed include: the impact of the transition tax, the revaluation of deferred tax assets and liabilities to reflect the 21% corporate tax rate, and the impact to the aforementioned items on state income taxes. We have completed our accounting for the income tax effects under the Tax Act that are relevant to us and required to be recorded and disclosed pursuant to FASB ASC 740, Income Taxes. Accordingly, any and all provisional amounts previously recorded in accordance with SEC Staff Accounting Bulletin No. 118 have been adjusted to reflect their final amounts.

Beginning in 2018, the GILTI provisions in the Tax Act require us to include, in our U.S. income tax return, foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. Per guidance issued by the FASB, companies can either account for deferred taxes related to GILTI or treat tax arising from GILTI as a period cost. Both are acceptable methods subject to an accounting policy election. On December 31, 2018, we finalized our policy and have elected to use the period cost method for GILTI. In 2018, we did not incur any GILTI inclusion as our foreign subsidiaries generated losses.

The BEAT provisions in the Tax Act eliminate the deduction of certain base-erosion payments made to related foreign corporations, and impose a minimum base erosion anti-abuse tax if greater than regular tax. In 2018, our company was not subject to BEAT as it did not meet the requirements to be subject to BEAT.

Note 13. Commitments and Contingencies

Operating Leases

Our headquarters are located in Redwood City, California, where we occupy approximately 107,200 square feet of office and laboratory space in four buildings within the same business park of Metropolitan Life Insurance Company ("MetLife"). Our lease ("Lease") with MetLife includes approximately 28,200 square feet of space located at 200 and 220 Penobscot Drive, Redwood City, California (the "Penobscot Space"), approximately 37,900 square feet of space located at 400 Penobscot Drive, Redwood City, California (the "Building 2 Space"), approximately 11,200 square feet of space located at 501 Chesapeake Drive, Redwood City, California (the "501 Chesapeake Space"), and approximately 29,900 square feet of space located at 101 Saginaw Drive, Redwood City, California (the "Saginaw Space").

We entered into the initial lease with MetLife for a portion of this space in 2004 and the lease has been amended multiple times since then to adjust space and amend the terms of the Lease, with the lease amendment ("Seventh Amendment") in October 2016 which, for one of our buildings, waived our existing asset retirement obligation, and extended the lease term to January 2022. The various terms for the spaces under the lease have expiration dates that range from January 2020 through January 2022. Beginning in February 2014, we have subleased certain office and laboratory space to different subtenants with separate options to extend the subleases. These subleases will expire in November 2019.

In February 2019, we entered into the eighth amendment to the Lease ("Eighth Amendment") with MetLife to extend the lease terms for the Penobscot Space, the Building 2 Space and the Chesapeake Space for another 88 months. The lease on the Saginaw Space will expire in January 2020. The lease terms for the Penobscot Space and Building 2 Space have an expiration date of May 2027. The lease term for the 501 Chesapeake Space has an expiration date of May 2029. Refer to Note 16, "Subsequent Events" for more details.

We incurred $3.6 million of capital improvement costs related to the facilities leased from MetLife through December 31, 2012. During 2011 and 2012, we requested and received $3.1 million of reimbursements from the landlord for the tenant improvement and HVAC allowances for the completed construction. The reimbursements were recorded once cash was received and are amortized on a straight line basis over the term of the lease as a reduction in rent expense. The remaining lease incentive obligations were $0.5 million and $0.9 million at December 31, 2018 and 2017, respectively, and are reflected as liabilities on the consolidated balance sheets. Rent expense for the Redwood City

properties is recognized on a straight-line basis over the term of the lease.

We are required to restore certain areas of the Redwood City facilities that we are renting to their original form. We are expensing the asset retirement obligation over the terms of the respective leases. We review the estimated obligation each reporting period and make adjustments if our estimates change. We recorded asset retirement obligations of $0.2 million as of December 31, 2018 and 2017, which are included in other liabilities on the consolidated balance sheets. Accretion expense related to our asset retirement obligations was nominal in 2018 and 2017.

Pursuant to the terms of the 7th amended lease agreement, we exercised our right to deliver a letter of credit in lieu of a security deposit. The letter of credit is collateralized by deposit balances held by the bank in the amount of $0.7 million as of December 31, 2018 and 2017, which is recorded as non-current restricted cash on the consolidated balance sheets. See Note 13, “Commitments and Contingencies.” Pursuant to the terms of the Eighth Amendment, the amended letter of credit in the amount of $1.1 million is collateralized by deposit balances held by the bank in 2019. Rent expense was $3.2 million, $3.2 million and $2.9 million in 2018, 2017 and 2016, respectively, partially offset by sublease income of $1.1 million, $1.4 million and $1.2 million, respectively.

Capital Leases

In December 2016, we entered into a three-year financing lease agreement with a third party supplier for the purchase of laboratory equipment that was partially financed through a capital lease of approximately $0.4 million. The lease became effective upon delivery of the equipment, which occurred in February 2017, and the term of the lease is three years from the effective date. This financing agreement was accounted for as a capital lease due to the bargain purchase option at the end of the lease.

In April 2017, we entered into a three-year financing lease agreement with a third party supplier for the purchase of information technology equipment for approximately $0.3 million. The effective date of the lease was May 19, 2017 and the term of the lease is three years. This financing agreement was accounted for as a capital lease due to the bargain purchase option at the end of the lease.

Leases

Future minimum payments under non-cancellable capital and operating leases at December 31, 2018 are as follows (in thousands):

Years ending December 31,	Capital Leases	Operating Leases
2019	$ 252	$ 3,280
2020	61	712
2021	—	490
2022	—	41
2023	—	—
Total minimum lease payments [1]	313	$ 4,523
Less: amount representing interest	(10)	
Present value of capital lease obligations	303	
Less: current portion	(242)	
Long-term portion of capital leases	$ 61	

(1) Minimum payments have not been reduced by future minimum sublease rentals of $0.9 million to be received under non-cancellable subleases.

Other Commitments

We enter into supply and service arrangements in the normal course of business. Supply arrangements are primarily for fixed-price manufacture and supply. Service agreements are primarily for the development of manufacturing processes and certain studies. Commitments under service agreements are subject to cancellation at our discretion which may require payment of certain cancellation fees. The timing of completion of service arrangements is subject to variability in estimates of the time required to complete the work.

The following table provides quantitative data regarding our other commitments. Future minimum payments reflect amounts that we expect to pay including potential obligations under services agreements subject to risk of cancellation by us (in thousands):

Other Commitment Agreement Type	Agreement Date	Future Minimum Payment
Manufacture and supply agreement with expected future payment date of December, 2022	April 2016	$ 1,458
Service agreement for stability study	July 2017	331
Service agreement for clinical trial	December 2017	1,258
Total other commitments		$ 3,047

Credit Facility

Effective June 30, 2017, we entered into a credit facility (the "Credit Facility") consisting of term loans ("Term Debt") totaling up to $10.0 million, and advances ("Advances") under a revolving line of credit ("Revolving Line of Credit") totaling up to $5.0 million with an accounts receivable borrowing base of 80% of eligible accounts receivable. At December 31, 2018, we have not drawn from the Credit Facility. In September 2018, we entered into a Fourth Amendment to the Credit Facility whereby the draw period on the term debt was extended to September 30, 2019. We may draw on the Term Debt at any time prior to September 30, 2019, subject to customary conditions for funding including, among others that no event of default exists. We may draw on the Revolving Line of Credit at any time prior to the maturity date. On October 1, 2022, any loans for Term Debt mature and the Revolving Line of Credit terminates. The Term Debt bears interest through maturity at a variable rate based on the London Interbank Offered Rate plus 3.60%. Advances under the Revolving Line of Credit bear interest at a variable annual rate equal to the greater of (i) 1.00% above the prime rate and (ii) 5.00%.

The Credit Facility allows for interest-only payments on the Term Debt through November 1, 2020. Monthly payments of principal and interest on the Term Debt are required following the applicable amortization date. We may elect to prepay in full the Term Debt and Advances under the Revolving Line of Credit at any time. Prepayments of Term Debt and early termination of the Revolving Line of Credit are subject to prepayment and final payment fees are as follows:

	Term Debt	Revolving Line of Credit
Through and including the first anniversary of the funding date of the first Term Debt drawn	2.0%	
After the first anniversary of the funding date of the first Term Debt drawn and before the maturity date	1.0%	
On the earliest to occur of the maturity date, the acceleration of Term Debt drawn or prepayment of Term Debt drawn	5.5%	
Through and including the first anniversary of the closing date		3.0%
After the first anniversary of the closing date through and including the second anniversary of the closing date		2.0%
After the second anniversary of the closing date through and including the third anniversary of the closing date		1.0%

Our obligations under the Credit Facility are secured by a lien on substantially all of our personal property other than our intellectual property. The Credit Facility includes a number of customary covenants and restrictions which require us to comply with certain financial covenants including achieving consolidated product revenues levels at minimum levels as set forth in the Credit Facility through December 2018 and on and after January 2019, in each case unless we maintain certain minimum cash levels with the lender in an amount equal to or greater than six times the sum of the average six-month trailing operating cash flow net outlay plus the average monthly principal due and payable in the immediately succeeding three-month period. The Credit Facility places various restrictions on our company's transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens and selling assets and permitted assets to be held at

foreign subsidiaries above specified caps, in each case subject to certain exceptions. A failure to comply with these covenants could permit the lender to exercise remedies against us and the collateral securing the Credit Facility, including foreclosure of our properties securing the Credit Facilities and our cash. At December 31, 2018, we were in compliance with the covenants for the Credit Facility.

As further discussed in Note 16, “Subsequent Events”, in February 2019, we entered into the eighth lease amendment of our business premises (the “Eighth Amendment”). Pursuant to the terms of the Eighth Amendment, we exercised an option to deliver a $1.1 million letter of credit to the lessor in lieu of a security deposit. In January 2019, we entered into the Fifth Amendment to the Credit Facility, which amended certain restrictive covenants with respect to letters of credit made in connection with the leasing of real property.

Legal Proceedings

We are not currently a party to any material pending litigation or other material legal proceedings.

In February 2018, we and EnzymeWorks, Inc. (U.S.), Suzhou Hanmei Biotechnology Co. Ltd, d/b/a EnzymeWorks, Inc. (China) (collectively, "EnzymeWorks"), Junhua Tao, and Andrew Tao reached a settlement concerning the lawsuit filed by us in February 2016 against EnzymeWorks, Junhua Tao, and Andrew Tao in the United States District Court for the Northern District of California. The parties have entered into a settlement agreement, the terms of which are confidential. The parties have also stipulated to a judgment of patent infringement of all asserted patents against EnzymeWorks, and a permanent injunction barring any future infringement. The remaining claims against EnzymeWorks, and all claims against Junhua Tao, and Andrew Tao including trade secret misappropriation, breach of contract and voidable transfer have been dismissed with prejudice. EnzymeWorks appealed the sanctions levied against them by Judge Orrick to the Federal Circuit and filed its opening brief on May 30, 2018. On July 9, 2018, Codexis filed its response brief, and EnzymeWorks filed its reply on July 30, 2018. On February 8, 2019, the Federal Circuit panel of judges assigned to the case issued an opinion affirming the lower court’s ruling and remanding the case to the lower court on jurisdictional grounds to vacate the order to which the parties had earlier stipulated.

Indemnifications

We are required to recognize a liability for the fair value of any obligations we assume upon the issuance of a guarantee. We have certain agreements with licensors, licensees and collaborators that contain indemnification provisions. In such provisions, we typically agree to indemnify the licensor, licensee and collaborator against certain types of third party claims. The maximum amount of the indemnifications is not limited. We accrue for known indemnification issues when a loss is probable and can be reasonably estimated. There were no accruals for expenses related to indemnification issues for any periods presented.

Note 14. Related Party Transactions

Exela PharmSci, Inc. (“Exela”)

We entered into a commercialization agreement with Exela in 2007. Under the license agreement, as amended, we and Exela cross-licensed certain technology relating to the manufacture of argatroban, an API, in exchange for rights to certain sublicensing fees or development payments and profit sharing. The revenue sharing arrangement was terminated in December 2017.

Thomas R. Baruch, one of our directors, serves on the board of directors of Exela, and is a retired general partner in Presidio Partners 2007, L.P., which owns over 10% of Exela’s outstanding capital stock. As such, Mr. Baruch has an indirect pecuniary interest in the shares of Exela held by Presidio Partners 2007, L.P.

We had no revenue from transactions with Exela in 2018. We recognized $2.6 million in 2017 and $2.2 million in 2016 as research and development revenue from transactions with Exela. We had no receivables at December 31, 2018 and $1.6 million of receivables due from Exela at December 31, 2017.

AstraZeneca PLC

Pam P. Cheng, a member of our board of directors, joined AstraZeneca PLC as Executive Vice President, Operations and Information Technology in June 2015. We sell biocatalyst products to AstraZeneca PLC, to Alfa Aesar, which is a purchasing agent of AstraZeneca PLC, and also to Asymchem Life Science Co, Ltd, which is a contract manufacturer for AstraZeneca PLC.

We recognized product revenue of $0.6 million in 2018, $0.1 million in 2017 and de minimis revenue in 2016 from transactions with AstraZeneca PLC. We recognized no revenue from transactions with Alfa Aesar in 2018 and 2017 and $0.4 million of product revenue in 2016. We recognized de minimis revenue from Asymchem Life Science Co, Ltd in 2018, $75 thousand in 2017, and de minimis revenue in 2016. At December 31, 2018, we had $0.2 million of receivables and at December 31, 2017,

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we had $0.1 million of receivables due from AstraZeneca, PLC. At December 31, 2018, we had no receivables and at December 31, 2017, we had $0.1 million of receivables due from Asymchem Life Science Co, Ltd. At December 31, 2018 and 2017, we had no receivables due from Alfa Aesar.

Note 15. Segment, Geographical and Other Revenue Information
Segment Information

As discussed in Note 2, "Basis of Presentation and Summary of Significant Accounting Policies," beginning in 2018, we identified our biotherapeutics business as a standalone business segment. Our two reportable business segments as of January 1, 2018, consisted of Performance Enzymes and Novel Biotherapeutics.
We report corporate-related expenses such as legal, accounting, information technology, and other costs that are not otherwise included in our reportable business segments as "Corporate costs." All items not included in income (loss) from operations are excluded from the business segments.
We manage our assets on a total company basis, not by business segment, as the majority of our operating assets are shared or commingled. Our CODM does not review asset information by business segment in assessing performance or allocating resources, and accordingly, we do not report asset information by business segment.

Performance Enzymes
We initially commercialized our CodeEvolver® protein engineering technology platform and products in the pharmaceuticals market, and to date this continues to be our largest market served. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. We have also used the technology to develop customized enzymes for use in other industrial markets. These markets consist of several large industrial verticals, including food and food ingredients, animal feed, flavors, fragrances, and agricultural chemicals. We also use our technology to develop enzymes for customers using NGS and PCR/qPCR for in vitro molecular diagnostic and molecular biology research applications.

Novel Biotherapeutics
We are also targeting new opportunities in the pharmaceutical industry to discover, improve, and/or develop biotherapeutic drug candidates. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer’s pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity. Most notable is our lead program for the potential treatment of PKU in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we announced a strategic collaboration with Nestlé Health Science to advance CDX-6114, our own novel orally administrable enzyme therapeutic candidate for the potential treatment of PKU. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, which was conducted in Australia. In November 2018, we announced top-line results from the Phase 1a study in healthy volunteers with CDX-6114. In December 2018, Nestlé Health Science became obligated to pay us an additional $1.0 million within 60 days after the achievement of a milestone relating to formulation of CDX-6114. In January 2019, we received notice from the U.S. Food and Drug Administration (the “FDA”) that it had completed its review of our investigational new drug application (“IND”) for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license for the global development and commercialization of CDX-6114 for the management of PKU. The exercise of the option triggers a $3 million milestone payment. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019. See Note 16, “Subsequent Events” in the notes to the

Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for details.
We have also developed a pipeline of other biotherapeutic drug candidates in which we expect to continue to make additional investments with the aim of advancing additional product candidates targeting other therapeutic areas.

For the year ended December 31, 2018, primarily all revenues related to the Novel Biotherapeutics segment were generated from our collaboration with customer projects. There was no revenue related to the Novel Biotherapeutics segment in the year ended December 31, 2017. Novel Biotherapeutics had no operational activity in the year ended December 31, 2016.

Our CODM regularly reviews our segments and the approach provided by management for performance evaluation and resource allocation.

Operating expenses that directly support the segment activity are allocated based on segment headcount, revenue contribution or activity of the business units within the segments, based on the corporate activity type provided to the segment. The expense allocation excludes certain corporate costs that are separately managed from the segments. This provides the CODM with more meaningful segment profitability reporting to support operating decisions and allocate resources.

The following table provides financial information by our reportable business segments along with a reconciliation to consolidated loss before income taxes (in thousands):

	Year Ended December 31, 2018			Year Ended December 31, 2017		
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total
Revenues:						
Product revenue	$25,590	$ —	$25,590	$26,685	$ —	$26,685
Research and development revenue	21,483	13,521	35,004	15,648	7,691	23,339
Total revenues	47,073	13,521	60,594	42,333	7,691	50,024
Costs and operating expenses:						
Cost of product revenue	12,620	—	12,620	14,327	—	14,327
Research and development[1]	18,924	10,185	29,109	16,847	12,107	28,954
Selling, general and administrative	7,538	771	8,309	7,371	—	7,371
Total segment costs and operating expenses	39,082	10,956	50,038	38,545	12,107	50,652
Income (loss) from operations	$7,991	$ 2,565	$10,556	$3,788	$ (4,416)	$(628)
Corporate costs [2]			(20,324)			(21,245)
Depreciation			(1,147)			(1,042)
Loss before income taxes			$(10,915)			$(22,915)

[1] Research and development expenses and Selling, general and administrative expenses exclude depreciation.
[2] Corporate costs include unallocated selling, general and administrative expense, interest income, and other income and expenses.

The following table provides stock-based compensation expense included in income (loss) from operations by segment (in thousands):

	2018			2017		
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total
Stock-based compensation	$2,591	$ 338	$2,929	$2,306	$ 208	$2,514

Significant Customers

Customers that each contributed 10% or more of our total revenues were as follows:

	Percentage of Total Revenues For The Years Ended December 31,		
	2018	2017	2016
Merck	29 %	28 %	47 %
Nestlé Health Science	22 %	15 %	*
Tate & Lyle	13 %	11 %	*
Novartis	*	14 %	*
GSK	*	*	22 %

Customers that each accounted for 10% or more of our accounts receivable balance for the period presented were as follows:

	Percentage of Accounts Receivables As Of December 31,	
	2018	2017
Merck	37 %	31 %
Nestlé Health Science	17 %	*
Tate & Lyle	*	16 %
Novartis	11 %	15 %
Kyorin Pharmaceutical Co Ltd	16 %	*
Exela PharmaSci, Inc.	*	14 %

* Percentage was less than 10%

Geographic Information

Geographic revenues are identified by the location of the customer and consist of the following (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Revenues			
Americas	$15,370	$15,575	$23,126
EMEA	22,361	19,610	17,138
APAC	22,863	14,839	8,573
Total revenues	$60,594	$50,024	$48,837

Identifiable long-lived assets by location and goodwill by reporting unit as of year-end were as follows (in thousands):

	December 31,	
	2018	2017
Long-lived assets		
United States	$4,759	$2,815

	December 31, 2018		
	Performance Enzymes	Novel Biotherapeutics	Total
Goodwill	$2,463	$ 778	$3,241

Note 16. Subsequent Events

Operating Leases

In February 2019, we entered into the eighth lease amendment ("Eighth Amendment") with MetLife to extend the lease term for the Penobscot Space, the Building 2 Space and the 501 Chesapeake Space for another 88 months. The various terms for these properties have expiration dates that range from May 2027 to May 2029. The terms include an optional renewal period of 5 years after the expiration date based on fair market rates for comparable transactions in the geographic area described in the Eighth Amendment. The Eighth Amendment requires us to install certain improvements to the buildings. On completion of the improvements to the building, the landlord will reimburse us up to a contractually specified amount and the landlord will become the owner of the improvements. Pursuant to the terms of the Eighth Amendment, we exercised our right to deliver a letter of credit in lieu of a security deposit. The letters of credit are collateralized by deposit balances held by the bank in the amount of $1.1 million in 2019. These deposits will be recorded as restricted cash on the consolidated balance sheets. Total future minimum lease payments under the Eighth Amendment is $32.9 million.

FDA Approval and Nestlé Health Science Exercises Option for Exclusive Global License to CDX-6114

In January 2019, we received notice from the U.S. Food and Drug Administration (the “FDA”) that it had completed its review of our investigational new drug application (“IND”) for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States.

In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sublicensable license to develop and commercialize certain products based on the our novel, orally delivered enzyme IND for the management of phenylketonuria. Nestlé Health Science was granted this option under the Development, Option and Licensing Agreement with Codexis announced in October 2017. The exercise of the option triggered a $3 million milestone payment from Nestlé Health Science to Codexis. Upon exercising its option, Nestlé Health Science has assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX - 6114-004, which is expected to be completed in the second quarter of 2019.

Selected Quarterly Financial Data (Unaudited)

The following table provides the selected quarterly financial data for 2018 and 2017:

Condensed Consolidated Statements of Operations

(In Thousands, Except Per Share Amounts)

	Quarter Ended [1]							
	December 31, 2018 [3]	September 30, 2018	June 30, 2018	March 31, 2018	December 31, 2017 [3]	September 30, 2017	June 30, 2017	March 31, 2017
Revenues:								
Product revenue	$7,299	$8,405	$3,723	$6,163	$7,551	$6,948	$6,600	$5,586
Research and development revenue	8,769	8,541	9,815	7,879	14,171	3,036	3,747	2,385
Total revenues	$16,068	$16,946	$13,538	$14,042	$21,722	$9,984	$10,347	$7,971
Costs and operating expenses:								
Cost of product revenue	$2,393	$3,791	$2,611	$3,825	$3,559	$3,976	$3,790	$3,002
Research and development	7,513	7,917	7,370	7,178	9,417	8,055	6,348	5,839
Selling, general and administrative	6,806	7,344	7,395	7,746	7,867	7,989	6,546	6,606
Total costs and operating expenses	$16,712	$19,052	$17,376	$18,749	$20,843	$20,020	$16,684	$15,447
Income (loss) from operations	$(644)	$(2,106)	$(3,838)	$(4,707)	$879	$(10,036)	$(6,337)	$(7,476)
Income (loss) before income taxes	$(486)	$(1,987)	$(3,746)	$(4,696)	$919	$(10,076)	$(6,322)	$(7,436)
Net income (loss)	$(461)	$(1,988)	$(3,735)	$(4,694)	$970	$(10,226)	$(6,280)	$(7,460)
Net income (loss) per share, basic	$(0.01)	$(0.04)	$(0.07)	$(0.10)	$0.02	$(0.21)	$(0.13)	$(0.18)
Net income (loss) per share, diluted	$(0.01)	$(0.04)	$(0.07)	$(0.10)	$0.02	$(0.21)	$(0.13)	$(0.18)
Weighted average common shares used in computing net income (loss) per share, basic [2]	53,973	53,597	52,787	48,385	48,187	48,147	47,232	41,250
Weighted average common shares used in computing net income (loss) per share, diluted[2]	53,973	53,597	52,787	48,385	50,599	48,147	47,232	41,250

(1) Amounts were computed independently for each quarter, and the sum of the quarters may not total the annual amounts due to rounding differences.

(2) The full year net loss per share of common stock, basic and diluted, may not equal the sum of the quarters due to weighting of outstanding shares.

(3) PSUs, PBOs, and cash bonus awards are granted to certain employees and executives and are subject to our performance in achieving pre-determined criteria approved by our board of directors. Based on the actual achievement of the annual goals, we updated the calculation of the annual expense in the fourth quarter which resulted in true-up adjustments of approximately $(0.5) million in 2018 and $0.1 million in 2017, primarily in selling, general and administrative expense.

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ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURES

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, under the supervision of our Chief Executive Officer and Chief Financial Officer and with the participation of our disclosure committee, evaluated the effectiveness of the design and operation of our disclosure controls and procedures as of December 31, 2018. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2018 at the reasonable assurance level.

Management’s Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with United States generally accepted accounting principles.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2018 based on the guidelines established in Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on the results of our evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2018. We reviewed the results of management’s assessment with our Audit Committee.

Our internal control over financial reporting as of December 31, 2018 has been audited by BDO USA, LLP, an independent registered public accounting firm, as stated in their report which is included in Item 8 of this Annual Report.

Inherent Limitations on Effectiveness of Controls

In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, even if determined effective and no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives to prevent or detect misstatements. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) identified in connection with the evaluation required by paragraph (d) of Rule 13a-15 or 15d-15 of the Exchange Act, which occurred during the fourth fiscal quarter of the year ended December 31, 2018, which has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Effective January 1, 2018, we adopted the provisions of Accounting Standards Update (ASU) 2014-09, "Revenue from Contracts with Customers (Topic 606) and the related amendments (“ASC 606”). In response, we have updated and enhanced our internal accounting processes and our internal controls over financial reporting to ensure that we

maintain adequate internal controls over financial reporting. This has required, and will continue to require, additional investments by us. There were no other significant changes to our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION
Not applicable.

PART III
ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE
The information required by this item concerning our directors, executive officers, compliance with Section 16 of the Exchange Act, our code of ethics and our Nominating and Corporate Governance Committee, and our Audit Committee is incorporated by reference from the information that will be set forth in the sections under the headings "Election of Directors," "Other Matters—Section 16(a) Beneficial Ownership Reporting Compliance" and "Corporate Governance Matters" in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission in connection with the Annual Meeting of Stockholders to be held in 2019 (the "2019 Proxy Statement").
ITEM 11. EXECUTIVE COMPENSATION
The information required by this item concerning executive compensation is incorporated by reference from the information that will be set forth in the 2019 Proxy Statement under the headings "Executive Compensation," and "Corporate Governance Matters."
ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS
The information required by this item concerning securities authorized for issuance under equity compensation plans and security ownership of certain beneficial owners and management is incorporated by reference from the information that will be set forth in the 2019 Proxy Statement under the headings "Executive Compensation—Equity Compensation Plan Information" and "Information Concerning Voting and Solicitation—Security Ownership of Certain Beneficial Owners and Management."
ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS,
AND DIRECTOR INDEPENDENCE
The information required by this item concerning transactions with related persons and director independence is incorporated by reference from the information that will be set forth in the 2019 Proxy Statement under the headings "Certain Relationships and Related Transactions" and "Corporate Governance Matters."
ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES
The information required by this item is incorporated by reference from the information that will be set forth in the 2019 Proxy Statement under the heading "Ratification of Independent Registered Public Accounting Firm—Principal Accounting Fees and Services."

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

1. Financial Statements: See “Index to Consolidated Financial Statements” in Part II, Item 8 of this Annual Report on Form 10-K
2. Exhibits: The exhibits listed in the accompanying index to exhibits are filed or incorporated by reference as part of this Annual Report on Form 10-K.

ITEM 16. FORM 10-K SUMMARY

None.

EXHIBIT INDEX

Exhibit No.	Description
3.1	Amended and Restated Certificate of Incorporation of Codexis, Inc. filed with the Secretary of the State of the State of Delaware on April 27, 2010 and effective as of April 27, 2010 (incorporated by reference to Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2010, filed on May 28, 2010).
3.2	Certificate of Designations of Series A Junior Participating Preferred Stock of Codexis, Inc., filed with the Secretary of State of the State of Delaware on September 4, 2012 (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on September 4, 2012).
3.3	Amended and Restated Bylaws of Codexis, Inc. effective as of April 27, 2010 (incorporated by reference to Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2010, filed on May 28, 2010).
4.1	Reference is made to Exhibits 3.1 through 3.3.
4.2	Form of the Company's Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on From 10-Q for the quarter ended June 30, 2012, filed on August 9, 2012).
10.1A*	Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of February 1, 2004.
10.1B*	Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of June 1, 2004.
10.1C*	Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of March 9, 2007.
10.1D*	Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of March 31, 2008.
10.1E	Fourth Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of September 17, 2010 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2010, filed on November 4, 2010).
10.1F	Fifth Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of March 16, 2011 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2011, filed on May 6, 2011).
10.1G	Sixth Amendment to Lease by and between the Company and Metropolitan Life Insurance Company dated as of September 27, 2012 (incorporated by reference to Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2012, filed on November 7, 2012).
10.1H	Seventh Amendment to Lease by and between the Company and Metropolitan Life Insurance Company dated as of October 11, 2016 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report

	on Form 10-Q for the quarter ended September 30, 2016, filed on November 8, 2016).
10.2+*	Codexis, Inc. 2002 Stock Plan, as amended, and Form of Stock Option Agreement.
10.3+*	Codexis, Inc. 2010 Equity Incentive Award Plan and Form of Stock Option Agreement.
10.4*	Form of Indemnification Agreement between the Company and each of its directors, officers and certain employees.
10.5A+*	Form of Change of Control Severance Agreement between the Company and certain of its officers.

Exhibit No.	Description
10.5B+	Form of Amended and Restated Change of Control Severance Agreement by and between Codexis, Inc. and certain of its officers (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, filed on October 14, 2016).
10.5C+	Form of Amendment to Change of Control Severance Agreement by and between Codexis, Inc. and certain of its officers (incorporated by reference to Exhibit 10.5 to the Company's Annual Report on Form 10-K for the year ended December 31, 2017, filed March 15, 2018).
10.6	Asset Purchase Agreement, dated October 28, 2010, by and among the Company, Codexis Mayflower Holdings, LLC and Maxygen, Inc. (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K, filed on October 28, 2010).
10.7A†	Manufacture and Supply Agreement, dated May 16, 2011, by and between the Company and Lactosan GmbH & Co. KG (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2011, filed on August 3, 2011).
10.7B	Amendment No. 1 to the Manufacture and Supply Agreement by and between the Company and Lactosan GmbH & Co. KG dated as of March 9, 2012 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2012, filed on May 10, 2012).
10.8A+	Offer Letter, dated as of October 12, 2016, by and between the Company and Michael Aldridge (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016).
10.8B+	Separation Agreement by and between Michael Aldridge and the Company, dated August 17, 2018.
10.9+	Offer Letter Agreement by and between the Company and Gordon Sangster effective as of July 11, 2014 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 31, 2014, filed on November 6, 2014).
10.10A+	Employment Agreement by and between the Company and John Nicols effective as of May 28, 2012 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, filed on August 9, 2012).
10.10B+	John Nicols Stock Option Grant Notice and Stock Option Agreement dated June 13, 2012 between John J. Nicols and the Company (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, filed on August 9, 2012).
10.10C+	John Nicols Restricted Stock Grant Notice and Restricted Stock Agreement dated June 13, 2012 between John J. Nicols and the Company (incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, filed on August 9, 2012).
10.10D+	Amendment to Employment Agreement between the Company and John Nicols, dated April 21, 2016 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2016).

10.10E+	Amendment to Employment Agreement between the Company and John Nicols, dated November 16, 2017 (incorporated by reference to Exhibit 10.8E to the Company's Annual Report on Form 10-K for the year ended December 31, 2017, filed on March 15, 2018).
10.11A†	Sitagliptin Catalyst Supply Agreement by and between Merck Sharp and Dohme Corp. and the Company dated as of February 1, 2012 (incorporated by reference to Exhibit 10.25 to the Company's Annual Report on Form 10-K for the year ended December 31, 2012, filed on April 2, 2013).
10.11B†	Amendment to Sitagliptin Catalyst Supply Agreement between Merck Sharp and Dohme Corp. and the Company dated as of October 1, 2013 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2013, filed on November 12, 2013).
10.11C	Amendment No. 2 to Sitagliptin Catalyst Supply Agreement between Merck Sharp and Dohme Corp. and the Company dated as of February 25, 2015 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, filed on May 7, 2015).

Exhibit No.	Description
10.11D	Amendment No. 3 to Sitagliptin Catalysts Supply Agreement between Merck Sharp and Dohme Corp. and the Company dated as of December 17, 2015 (incorporated by reference to Exhibit 10.11D to the Company's Annual Report on Form 10-K for the year ended December 31, 2015, filed on March 8, 2016).
10.11E	Amendment No. 4 to Sitagliptin Catalysts Supply Agreement, effective as of January 1, 2016, by and between the Company and Merck Sharp and Dohme Corp. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, filed on November 8, 2016).
10.12A†	Global Development, Option and License Agreement by and among the Company, Nestec Ltd. and Nestlé Health Science S.A., effective as of October 12, 2017 (incorporated by reference to Exhibit 10.10 to the Company's Annual Report on Form 10-K for the year ended December 31, 2017).
10.12B†	Amendment No. 1 to Global Development, Option and License Agreement by and among the Company, Nestec Ltd. and Nestlé Health Science S.A., effective as of July 26, 2018.
10.12C†	Letter Agreement to Global Development, Option and License Agreement by and among the Company, Nestec Ltd. and Nestle Health Science S.A., effective as of December 12, 2018.
10.13†	Platform Technology Transfer, Collaboration and License Agreement by and between the Company and GlaxoSmithKline Intellectual Property Limited, effective as of July 10, 2014 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 31, 2014, filed on November 6, 2014).
10.14†	Platform Technology Transfer and License Agreement by and between the Company and Merck Sharp & Dohme Corp., dated as of August 3, 2015 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 31, 2015, filed on November 6, 2015).
10.14A†	Amendment No. 1 to Platform Technology Transfer and License Agreement by and between the Company and Merck Sharp & Dohme Corp., dated as of October 10, 2018.
10.15†	Loan and Security Agreement effective as of June 30, 2017 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2017).
10.15A†	First Amendment to Loan and Security Agreement effective as of September 28, 2017 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017).
10.15B†	Second Amendment to Loan and Security Agreement effective as of November 7, 2017 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.15B to the Company's Annual Report on Form 10-K for the year ended December 31, 2017, filed March 15, 2018).
10.15C†	Third Amendment to Loan and Security Agreement by and between the Company and Western Alliance Bank dated as of June 29, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2018, filed August 9, 2018).

10.15D†	Fourth Amendment to Loan and Security Agreement effective as of September 28, 2018 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, filed November 9, 2018).
12.1	Statement Regarding the Computation of Ratio of Earnings to Fixed Charges.
21.1	List of Subsidiaries.
23.1	Consent of BDO USA, LLP, independent registered public accounting firm.
24.1	Power of Attorney (see signature page to this Annual Report on Form 10-K).

Exhibit No.	Description
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
32.1**	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. §1350.
101	The following materials from Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2018, formatted in Extensible Business Reporting Language (XBRL) includes: (i) Consolidated Balance Sheets at December 31, 2018 and December 31, 2017, (ii) Consolidated Statements of Income for the years ended December 31, 2018, December 31, 2017 and December 31, 2016, (iii) Consolidated Statements of Comprehensive Loss for the years ended December 31, 2018, December 31, 2017 and December 31, 2016, (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2018, December 31, 2017 and December 31, 2016, (v) Consolidated Statements of Stockholders' Equity for the years ended December 31, 2018, December 31, 2017 and December 31, 2016 and (vi) Notes to Consolidated Financial Statements.

+ Indicates a management contract or compensatory plan or arrangement.

† Confidential treatment has been granted for certain information contained in this exhibit. Such information has been omitted and filed separately with the Securities and Exchange Commission.

* Filed as exhibits to the registrant's Registration Statement on Form S-1 (File No. 333-164044), effective April 21, 2010, and incorporated herein by reference.

** Pursuant to Item 601(b)(32) of Regulation S-K this exhibit is furnished rather than filed with this report.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

CODEXIS, INC.

Date: March 1, 2019 By: /s/ John J. Nicols
President and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints John J. Nicols, Gordon T. B. Sangster, and Richard A. Sabalot, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE

/s/ John J. Nicols John J. Nicols	President, Chief Executive Officer and Director (Principal Executive Officer)	Date:	March 1, 2019
/s/ Gordon T. B. Sangster Gordon T. B. Sangster	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	Date:	March 1, 2019
/s/ Bernard J. Kelley Bernard J. Kelley	Chairman of the Board of Directors	Date:	March 1, 2019
/s/ Thomas R. Baruch Thomas R. Baruch	Chairman Emeritus, Director	Date:	March 1, 2019
/s/ Pam P. Cheng Pam P. Cheng	Director	Date:	March 1, 2019
/s/ Byron L. Dorgan Byron L. Dorgan	Director	Date:	March 1, 2019
/s/ Kathleen S. Glaub Kathleen S. Glaub	Director	Date:	March 1, 2019
/s/ David V. Smith David V. Smith	Director	Date:	March 1, 2019
/s/ Dennis P. Wolf Dennis P. Wolf	Director	Date:	March 1, 2019
/s/ Patrick Y. Yang Patrick Y. Yang	Director	Date:	March 1, 2019