

CODEXIS INC  
Form 10-K  
March 09, 2017

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

FORM 10-K  
(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934  
For the fiscal year ended: December 31, 2016  
 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 (I.R.S. Employer  
Incorporation or Organization) Identification No.)

200 Penobscot Drive, 94063  
Redwood City, California  
(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

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

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  No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 229.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting

company” in Rule 12b-2 of the Exchange Act (Check one):

Large accelerated filer” Accelerated filer

Non-accelerated filer ” Smaller reporting company ”

(Do not check if a  
smaller reporting  
company)

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

The aggregate market value of voting common stock held by non-affiliates of Codexis as of June 30, 2016 was approximately \$114.2 million based upon the closing price reported for such date on The NASDAQ Global Select Market.

As of February 28, 2017, there were 41,382,691 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 2017 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, 2016. 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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Codexis, Inc.  
Annual Report on Form 10-K  
For The Year Ended December 31, 2016  
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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,” “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 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.

Many companies have historically used naturally occurring proteins to produce or enhance goods used in everyday life. Despite the growing number of commercial applications of naturally occurring proteins across many industries, the inherent limitations of naturally-occurring proteins frequently restrict their commercial use. Through the application of our proprietary CodeEvolver<sup>®</sup> protein engineering technology platform, we are able to engineer novel proteins to overcome these restrictions, thereby adding value or opening up new prospects for our potential clients' products, processes or businesses. We have developed new proteins that are significantly more stable and/or active in our commercial applications than proteins derived from nature.

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<sup>®</sup> 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<sup>®</sup> 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 STRATEGY

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

Licensing our CodeEvolver<sup>®</sup> protein engineering technology platform. We intend to continue to pursue opportunities to license our CodeEvolver<sup>®</sup> 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.

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.

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 intend to continue to advance our own novel enzyme biotherapeutic candidate for the potential treatment of phenylketonuria ("PKU") disease. We have also invested in research and development in an effort to generate additional early stage novel biotherapeutic candidates.

Developing high-performance enzymes for use in diagnostic applications. We intend to offer high-performance enzymes to customers using next generation sequencing ("NGS") and polymerase chain reaction ("PCR/qPCR") for in vitro molecular diagnosis 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, product launch, commercial scale-up 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<sup>®</sup> protein engineering technology platform, to improve their manufacturing productivity and efficiency or outsourcing the manufacture of their intermediates and active pharmaceutical ingredients (APIs).

### Our Solutions for the Pharmaceutical Market

#### Small Molecule Manufacturing Cost Reduction

Our pharmaceutical customers, which include a majority of the largest global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. Our CodeEvolver<sup>®</sup> 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 Codexis to earn three

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US EPA Presidential Green Chemistry Challenge awards for improved pharmaceutical manufacturing processes over the last eleven years. 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<sup>®</sup> 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. For example, we may be able to use our technology to improve the activity, stability or immunogenicity of a customer's biotherapeutic drug candidate.

#### Partner-funded Biotherapeutic Product Development

We are using our platform technology to improve characteristics of our customers' pre-existing biotherapeutic drug candidates. In July 2016, we successfully completed our obligations under a collaborative research and development agreement with a leading global biopharmaceutical company. Under that agreement, we employed our CodeEvolver protein engineering platform technology to develop a novel enzyme for use in our partner's preclinical therapeutic development program. During this project, we earned success fees, associated milestone payments and research and development service revenues. In November 2016, we announced that our biopharmaceutical partner had exercised its option to secure a non-exclusive license to the novel enzyme developed by Codexis. As a result, Codexis could receive additional annual license fees from our biopharmaceutical partner. We continue to pursue this and other customers who could benefit by applying our CodeEvolver<sup>®</sup> protein engineering platform technology to improve the discovery and/or development of other biotherapeutics in partnership with Codexis

#### Self-funded Biotherapeutic Product Development

We are also using our platform technology to develop our own early stage, novel enzyme therapeutic product candidates. Our lead product candidate is an enzyme which we have engineered to be orally administered and are developing 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.

We continue to invest in the development of our preclinical therapeutic enzyme product candidate as a potential treatment of PKU. We have filed patent applications covering the composition of matter for our therapeutic enzymes and the use of these enzymes as a treatment for PKU. In addition to the PKU program, we have previously made, and expect to continue to make, modest additional investments with the aim of generating additional product candidates targeting other therapeutic areas.

#### Fine Chemicals Markets

Beyond the pharmaceutical industry, our CodeEvolver<sup>®</sup> protein engineering platform technology has enabled cost-savings for our partners in the fine chemicals markets, and the food industry in particular. In December 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. We are seeking to expand our protein catalyst offerings in the fine chemicals market within and beyond the food industry, including, for example, to the 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 will target improved library preparation for NGS users and is expected to be available in beta-test format in the second quarter of 2017.

#### Licensing Our CodeEvolver<sup>®</sup> Protein Engineering Technology Platform

Our CodeEvolver<sup>®</sup> 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<sup>®</sup> protein engineering technology platform to discover and develop novel

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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<sup>®</sup> protein engineering technology Platform Technology Transfer, Collaboration and License Agreement (“GSK CodeEvolver<sup>®</sup> Agreement”) on July 10, 2014 with GlaxoSmithKline Intellectual Property Development Limited, a subsidiary of GlaxoSmithKline plc (collectively, “GSK”).

The GSK CodeEvolver<sup>®</sup> Agreement allows GSK to use our proprietary CodeEvolver<sup>®</sup> protein engineering technology platform in the field of human healthcare.

Under the terms of the GSK CodeEvolver<sup>®</sup> Agreement, we granted to GSK a non-exclusive, worldwide license to use our CodeEvolver<sup>®</sup> protein engineering technology platform to develop novel enzymes for (a) the manufacture and commercialization of compounds, molecules and products for the treatment of any human disease or medically treatable human condition, (b) the prophylaxis, diagnosis or treatment of any human disease or medically treatable human condition, and (c) the research and development of compounds, molecules and products for the treatment of any human disease or medically treatable human condition (the “Field”). This license to GSK is exclusive for the use of our CodeEvolver<sup>®</sup> protein engineering technology platform to develop novel enzymes for the synthesis of small-molecule compounds owned or controlled by GSK (the “GSK Exclusive Field”). GSK has the right to grant sublicenses to affiliates of GSK and, in certain limited circumstances, to third parties. We also granted a license to GSK to make or have made products developed using our CodeEvolver<sup>®</sup> protein engineering technology platform, with a right to grant sublicenses solely to affiliates of GSK, contract manufacturing organizations and contract research organizations. This manufacturing license is exclusive in the GSK Exclusive Field and otherwise non-exclusive in the Field. The licenses granted by us to GSK are subject to certain limitations based on pre-existing contractual obligations that apply to the technology and intellectual property that is the subject of the license grants. In addition, GSK is prohibited from using our CodeEvolver<sup>®</sup> protein engineering technology platform to develop or produce any enzymes or other compounds for or on behalf of any third party except that GSK can exercise its license rights in connection with certain research and development programs jointly performed with a bona fide third party collaborator so long as GSK uses our CodeEvolver<sup>®</sup> protein engineering technology platform independently from the third party collaborator and complies with all of the other restrictions and obligations under the GSK CodeEvolver<sup>®</sup> Agreement.

Under the GSK CodeEvolver<sup>®</sup> Agreement, we transferred our CodeEvolver<sup>®</sup> protein engineering technology platform to GSK over a twenty-one-month period that began on July 10, 2014, the effective date of the GSK CodeEvolver<sup>®</sup> Agreement. 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<sup>®</sup> protein engineering technology platform has been installed at GSK’s Upper Merion, Pennsylvania site.

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<sup>®</sup> Agreement and that cover our CodeEvolver<sup>®</sup> protein engineering technology platform and certain enzymes useful in the Field. Any improvements to our CodeEvolver<sup>®</sup> protein engineering technology platform during the technology transfer period were included in the license grants from us to GSK.

Under the GSK CodeEvolver<sup>®</sup> Agreement, GSK owns (the “GSK-Owned Technology”) (a) any enzyme technology that was developed during a project under the GSK CodeEvolver<sup>®</sup> Agreement that used our CodeEvolver<sup>®</sup> 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<sup>®</sup> 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 CodeEvolve<sup>®</sup> 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<sup>®</sup> Agreement continues, unless earlier terminated, until the expiration of all payment obligations under the GSK CodeEvolver<sup>®</sup> Agreement. GSK can terminate the GSK CodeEvolver<sup>®</sup> Agreement by providing 90 days written notice to us.

In 2015, we completed Wave 1 and Wave 2 of the transfer of our CodeEvolver<sup>®</sup> protein engineering technology platform to GSK. In addition to the \$6.0 million upfront payment and \$5.0 million Wave 1 technology transfer milestone payment received from GSK in 2014, in 2015 we received a \$6.5 million technology transfer milestone payment from GSK for the successful completion of Wave 2. In April 2016, we completed the full transfer of the CodeEvolver<sup>®</sup> protein engineering platform technology and earned Wave 3 milestone revenue of \$7.5 million. We also 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.

In the third quarter of 2016, we earned the first milestone under the agreement related to the development of an enzyme for an already-commercialized product. In addition, we are eligible to receive royalties based on net sales, if any, of a limited set of products developed by GSK using the CodeEvolver<sup>®</sup> protein engineering technology platform. Merck

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

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

Under the terms of the Merck CodeEvolver<sup>®</sup> Agreement, we granted to Merck a non-exclusive worldwide license to use the CodeEvolver<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> protein engineering technology platform to discover any therapeutic enzyme, diagnostic product or vaccine. In addition, Merck is prohibited from using the CodeEvolver<sup>®</sup> 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<sup>®</sup> protein engineering technology platform.

Under the terms of the Merck CodeEvolver<sup>®</sup> Agreement, Merck paid us \$18.0 million in technology transfer up-front and milestone payments over the technology transfer period of 15 months from August 3, 2015, the effective date of the Merck CodeEvolver<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup>-developed enzyme. The payments will be based on the total volume of API produced using the CodeEvolver<sup>®</sup>-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<sup>®</sup> Agreement, we transferred the CodeEvolver<sup>®</sup> 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<sup>®</sup> Agreement and that cover the CodeEvolver<sup>®</sup> protein engineering technology platform. Any improvements to the CodeEvolver<sup>®</sup> 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

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improvements to the CodeEvolver<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> Agreement using the CodeEvolver<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> Agreement by providing 90 days written notice to us. We can terminate the Merck CodeEvolver<sup>®</sup> Agreement by providing 30 days written notice to Merck if we determine, pursuant to our contractual audit rights under the Merck CodeEvolver<sup>®</sup> Agreement, that Merck has repeatedly failed to make required payments to us and/or materially underpaid us an amount due under the Merck CodeEvolver<sup>®</sup> Agreement. In the event the Merck CodeEvolver<sup>®</sup> 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<sup>®</sup> Agreement contains indemnification provisions under which Merck and we have agreed to indemnify each other against certain third party claims.

As of December 31, 2015, we completed Wave 1 of the transfer of our CodeEvolver<sup>®</sup> protein engineering technology platform to Merck. In 2015, we received from Merck a \$5.0 million upfront payment and a \$5.0 million Wave 1 technology transfer milestone payment. 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.

#### 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
- flexibility to apply at any point across their product’s lifecycle

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

In addition to products, we also offer R&D services to our customers. These R&D 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 been already been engineered, scaled up, and installed in a customer's commercial process. For example, we sell protein catalysts to Merck

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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 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 chemical 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 their own screening, they can send us their starting materials and desired chemical reaction, and we will test against our existing libraries of enzymes on an R&D 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 optimized enzymes that have been engineered specifically to perform a desired process according to a highly selective set of specifications. We typically charge customers on an R&D services basis by project or project-month. These are typically larger R&D 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 ranks 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, 2016, we owned or controlled approximately 600 issued patents and approximately 280 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. Our current intellectual property rights have terms that expire between 2017 and 2036. Our United States intellectual property rights directed to the CodeEvolver<sup>®</sup> 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<sup>™</sup> 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.

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.

As of December 31, 2016, 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<sup>®</sup>, Codex<sup>®</sup>, CodeEvolver<sup>®</sup>, Mosaic<sup>®</sup>, Sage<sup>™</sup>, MicrocypMYCP<sup>®</sup>, ProSAR<sup>™</sup>, Transform Your Thinking<sup>™</sup>, and a Codexis design mark (i.e., the Codexis logo).

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. For example, in February 2016, we filed a complaint against EnzymeWorks, Inc., a California corporation, EnzymeWorks, Inc., a Chinese corporation, and Junhua “Alex” Tao (collectively, the “Defendants”), alleging that the Defendants have engaged in willful patent infringement, trade secret misappropriation, breach of contract, intentional interference with contractual relations, intentional interference with prospective economic relations and statutory and common law unfair competition. The outcome of the case and the timing of its resolution are uncertain. For further information regarding this litigation, see Item 3, “Legal Proceedings.” Our litigation against the Defendants and any other 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.

## COMPETITION

### Overview

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, c-LEcta GmbH, Gingko Bioworks 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 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 Kuvadin in the United States, Europe and Japan for the treatment of a certain type of PKU. BioMarin has also recently completed a phase III clinical trial for an injectable enzyme substitution therapy for the potential treatment of PKU. Shire Plc, Genzyme / Sanofi S.A. and other companies market or are actively developing new biotherapeutics. 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 offering whole cell 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 is located in Redwood City, California and provides general administrative support to our business and is 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<sup>®</sup> 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 to our consolidated financial statements appearing in Item 8 of this Annual Report on Form 10-K for a description of our revenue 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 two locations, at our in-house facility in Redwood City, California and at a third-party contract manufacturing organization, Lactosan, GmbH & Co. KG (“Lactosan”), in Kapfenberg, Austria. In late 2015, we commenced manufacturing certain enzymes at another third-party contract manufacturing organization in Western Europe. 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.

### 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,					
	2016		2015		2014	
Customers:						
Merck	47	%	29	%	24	%
GSK	22	%	20	%	17	%
Exela	*		12	%	21	%

\* Percentage was less than 10%

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## EMPLOYEES

As of December 31, 2016, we had 106 full-time employees and two part-time employees worldwide. Of these employees, 61 were engaged in research and development, 16 were engaged in operations and quality control, and 29 were engaged in selling, general and administrative activities. None of our employees are 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](http://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's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding our filings, at [www.sec.gov](http://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

We have a limited operating history and have recently experienced significant changes to our business, 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. Since 2005, we have continued to generate revenues, but because our revenue growth has occurred in recent periods, our limited operating history may make it difficult to evaluate our current business and predict our future performance. Additionally, 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<sup>®</sup> cellulase enzymes program, and that we had stopped further development of our CodeXol<sup>®</sup> detergent alcohols program in the third quarter of 2013. 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 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 ability to deploy our technology platform in the in vitro molecular diagnostics market;
- 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 find a partner for or otherwise advance our biotherapeutic program;

- 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;
- our ability to implement and 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;
- our or our customers' ability to obtain regulatory approval for the sale and manufacturing of food products using our enzymes;
- 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; 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 \$8.6 million in 2016, \$7.6 million in 2015 and \$19.1 million in 2014. As of December 31, 2016 and 2015, we had an accumulated deficit of \$292.1 million and \$283.5 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 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 and Merck 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 or Merck, or if we fail to maintain our agreements with our collaborators, we may not be able to commercialize our existing and potential products, grow our business or generate sufficient revenues to support our operations, 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:

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- 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;
- 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 undergo 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, 2016, customers that each individually contributed 10% or more of our net revenue accounted for 69% of our total revenues. For the year ended December 31, 2015, customers that each contributed 10% or more of our net revenue accounted for 61% of our total revenues. 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. In addition, our revenue sharing arrangement, which is based on sales of the anticoagulant drug argatroban by our revenue sharing partner Exela PharmSci, Inc. ("Exela"), has declined in recent years and may decline in future periods due to increased competition resulting from the expiration of a third party patent related to the production of argatroban in June 2014.

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 two locations: our in-house facility in Redwood City, California; and at a third-party contract manufacturing organization, Lactosan, GmbH & Co. KG ("Lactosan"), in Kapfenberg, Austria. In late 2015, we commenced manufacturing certain enzymes at another third-party contract manufacturing organization in Western Europe. 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. We have experienced manufacturing delays at Lactosan in the past, including as recently as the second half of 2014. 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 one other contract manufacturer. 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 efforts to deploy our technology platform in the fine chemicals market may fail.

We have recently begun to use our CodeEvolver<sup>®</sup> 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 revenue 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, 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 Tate & Lyle decides to delay or discontinue developing its food ingredient product for which we signed an enzyme supply agreement in December 2016, 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.

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

We have recently begun to use our CodeEvolver<sup>®</sup> 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 revenue and cash flows from these activities. The failure to successfully and timely deploy products in this space may limit our growth and have a material adverse effect on our financial condition, operating results and business prospects.

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, 2016, we owned or controlled approximately 600 issued patents and approximately 280 pending patent applications in the United States and in various foreign jurisdictions. Our intellectual property rights, as of December 31, 2016, have terms that expire between 2017 and 2036. 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 may be required to file infringement claims, which can be expensive and time-consuming. For example, in February 2016, we filed a complaint against EnzymeWorks, Inc., a California corporation, EnzymeWorks, Inc., a Chinese corporation, and Junhua “Alex” Tao (collectively, the “Defendants”), alleging that the Defendants have engaged in, among other things, willful patent infringement, trade secret misappropriation and breach of confidence. 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 (including our litigation against the Defendants), 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 marketable 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.

Our biotherapeutic programs are early stage, highly regulated and expensive. Our ability to obtain 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 novel biotherapeutic candidates, in particular our novel oral enzyme product candidate for the treatment of PKU. Our efforts to advance our PKU program are subject to numerous risks, including the following:

- Our efforts to use CodeEvolver® protein engineering technology platform to generate new lead biotherapeutic candidates may not be successful in creating candidates of value.

- The successful development of biotherapeutic candidates is full of risk and uncertainty, requires long timelines and may lead to uncertain results, is highly regulated and may require expertise and capital resources we do not currently possess.

- If we are not successful in obtaining a partner to assist us with the funding and development of our PKU program, we may not have sufficient funds or expertise to advance development of the program on our own.

- To obtain regulatory approval to market our 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 do not have 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 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 our product candidate.

- The results of animal studies of our product candidate may not be predictive of future study results.

- If we begin clinical trials for our product candidate, we may find it difficult to enroll patients in our clinical trials given the limited number of patients that have PKU. Any enrollment difficulties could delay clinical trials and any potential product approval.

- Drug development is a highly regulated process. In particular, the regulatory approval process of the FDA and comparable foreign authorities is lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidate, our business will be harmed.

- 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 our PKU product candidate, if approved.

- 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 our product candidate, if approved.

- 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 \$2.4 million as of December 31, 2016.

- 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

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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 long-lived assets for impairment as of December 31, 2016. Based on our analysis, we determined that the fair value of the assets exceeded their carrying value and that no impairment was necessary as of December 31, 2016. 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.

If we are unable to implement and 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 and timely report our financial position, results of operations or cash flows 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.

We are dependent upon information technology systems, infrastructure and data. The multitude and complexity of our computer systems make them inherently vulnerable to service interruption or destruction, malicious intrusion and random attack. Likewise, data privacy or security breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, customers or other business partners may be exposed to unauthorized persons or to the public. Cyberattacks are increasing in their frequency, sophistication and intensity. Cyberattacks could include the deployment of harmful malware, denial-of-service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our business partners face similar risks and any security breach of their systems could adversely affect our security posture. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches.

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.

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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.

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 product for which we signed a supply agreement with Tate & Lyle is, 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.

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 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 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, c-LEcta GmbH, Gingko Bioworks 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 Kuvadin in the United States, Europe and Japan for the treatment of a certain type of PKU. BioMarin has also recently completed a phase III clinical trial for an injectable enzyme substitution therapy for the potential treatment of PKU. Shire Plc, Genzyme / Sanofi S.A. and other companies market or are actively developing new biotherapeutics. 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.

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, 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 Internal Revenue 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 Internal Revenue 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, 2016, our officers, directors and stockholders who hold at least 5% of our stock together beneficially own approximately 45% 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, 2016, two stockholders beneficially owned approximately 26% of our common stock in the aggregate.

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 marketable 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.

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 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 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”), and approximately 29,900 square feet of space located at 101 Saginaw Drive, Redwood City, California (the “Saginaw Space”). The term of the lease of the Penobscot Space, the Building 2 Space and the Saginaw Space lasts until January 31, 2020, and we have options to extend for two additional five year periods. In February 2014, we agreed to sublease approximately 26,500 square feet of the Saginaw Space to a subtenant for a period of three years. The subtenant has exercised an option to extend the sublease term until April 14, 2018, and the subtenant has one more option to extend the sublease term for an additional period of one year. In January 2015, we agreed to sublease approximately 3,400 square feet of the Saginaw Space to a subtenant for a period ending May 31, 2017 and the subtenant has an option to extend the sublease term for such portion of the Saginaw Space until September 30, 2019. In October 2015, we agreed to sublease approximately 20,200 square feet of the Penobscot Space to a subtenant through November 30, 2019.

We also lease approximately 11,200 square feet of space located at 501 Chesapeake Drive, Redwood City, California (the “501 Chesapeake Space”). In September 2012, we entered into a Sixth Amendment to Lease (the “Sixth Amendment”) with MetLife with respect to the 501 Chesapeake Space to extend the term of the lease of the 501 Chesapeake Space to January 31, 2017. Pursuant to the Sixth Amendment, we have two consecutive options to extend the term of the lease for the 501 Chesapeake Space for an additional period of five years per option. In October 2016, we entered into the Seventh Amendment to Lease pursuant to which we exercised the first of our options to extend the term of the lease for the 501 Chesapeake Space for an additional five years, commencing on February 1, 2017 and expiring on January 31, 2022.

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

On February 19, 2016, we filed a complaint against EnzymeWorks, Inc., a California corporation, EnzymeWorks, Inc., a Chinese corporation, and Junhua “Alex” Tao (collectively, the “Defendants”) in the United States District Court for the Northern District of California. The complaint alleges that the Defendants have engaged in willful patent infringement, trade secret misappropriation, breach of confidence, intentional interference with contractual relations, intentional interference with prospective economic relations and statutory and common law unfair competition. We have sought injunctive relief, monetary damages, treble damages, restitution, punitive damages and attorneys’ fees. On May 13, 2016, the Defendants filed a Partial Motion to Dismiss the claims for breach of contract, intentional interference with contractual relations, intentional interference with prospective economic relations, statutory unfair competition, and common law unfair competition in the First Amended Complaint. We opposed the Defendant’s Partial Motion to Dismiss. On August 11, 2016, the judge issued an order that denied the Defendants’ Partial Motion to Dismiss with respect to all five claims and in all relevant parts, and granted the motion with respect to certain underlying arguments. We are unable to determine when this litigation will be resolved or its ultimate outcome. Other than our litigation against the Defendants, we are not currently a party to any material litigation or other material legal proceedings.

#### 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 2016	High	Low
First Quarter	\$4.50	\$2.93
Second Quarter	4.34	3.00
Third Quarter	4.63	3.87
Fourth Quarter	5.25	4.31
Fiscal 2015	High	Low
First Quarter	\$4.59	\$2.50
Second Quarter	5.65	3.62
Third Quarter	4.62	3.02
Fourth Quarter	4.50	3.02

As of February 28, 2017, there were approximately 140 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.

## Dividend Policy

We have never declared or paid cash dividends on our common stock, and currently do not plan to declare dividends on shares of our common stock in the foreseeable future. We expect to retain our future earnings, if any, for use in the operation and expansion of our business. The payment of cash dividends in the future, if any, will be at the discretion of our board of directors and will depend upon such factors as earnings levels, capital requirements, our overall financial condition and any other factors deemed relevant by our board of directors.

## 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, 2011 through December 31, 2016. The figures represented below assume an investment of \$100 in our common stock at the closing price on December 31, 2011 and in the NASDAQ Composite Index and the NASDAQ Biotechnology Index on December 31, 2011 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.

\$100 investment in stock or index	Ticker	December 31,					
		2011	2012	2013	2014	2015	2016
Codexis, Inc.	CDXS	\$100.00	\$41.70	\$26.42	\$47.55	\$79.81	\$86.79
Nasdaq Composite Index	IXIC	\$100.00	\$117.45	\$164.57	\$188.84	\$201.98	\$219.89
Nasdaq Biotechnology Index	NBI	\$100.00	\$131.91	\$218.45			