COMPUGEN LTD
Form 20-F
March 07, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 20-F

o REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2015

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

o SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

DATE OF EVENT REQUIRING THIS SHELL COMPANY REPORT _____

COMMISSION FILE NO. 000-30902

_____

Compugen Ltd.
(Exact name of registrant as specified in its charter and translation of registrant's name into English)

_____

Israel
(Jurisdiction of incorporation or organization)

Azrieli Center, 26 Harokmim Street, Building D, Holon 5885849 Israel
(Address of principal executive offices)

_____

Ari Krashin, Chief Financial Officer
Phone: +972-3-765-8585, Fax: +972-3-765-8555

Azrieli Center, 26 Harokmim Street, Building D, Holon 5885849 Israel
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Ordinary shares, par value NIS 0.01 per share	The NASDAQ Stock Market LLC (The NASDAQ Global Market)

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None

(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report:

50,572,244 Ordinary Shares

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

o Yes x No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

o Yes x 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:

x Yes o 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 (232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

x Yes o No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of “accelerated filer and large accelerated filer” in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o Accelerated filer x Non-accelerated filer o

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP x

International Financial Reporting Standards as issued by the International Accounting Standards Board ¨

Other ¨

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.

Item 17 ¨ Item 18 ¨

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

o Yes x No

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CAUTIONARY STATEMENT REGARDING

FORWARD-LOOKING STATEMENTS

This annual report on Form 20-F includes “forward-looking statements” within the meaning of Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These statements include words such as “will,” “may,” “assume,” “expect,” “anticipate,” “could,” “project,” “estimate,” “possible,” “potential,” “believe “intend,”, and describe opinions about future events. We have based these forward-looking statements on information available to us as of the date hereof, and on our current assumptions, intentions, beliefs, expectations and projections about future events. We assume no obligation to update any such forward-looking statements. These forward-looking statements involve known and unknown risks and uncertainties that may cause the actual results, performance or achievements of Compugen to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Factors that could cause our actual results to differ materially from those projected in the forward-looking statements include, without limitation, the risk factors set forth under “Item 3. Key Information. Risk Factors,” the information about us set forth under “Item 4. Information about the Company” and information related to our financial condition under “Item 5. Operating and Financial Review and Prospects.”

All references in this annual report on Form 20-F to “Compugen,” the “Company,” “we,” “us,” “our,” or similar references re to Compugen Ltd. and our wholly owned subsidiary Compugen USA, Inc., except where the context otherwise requires or as otherwise indicated.

We have prepared our consolidated financial statements in United States dollars and in accordance with generally accepted accounting principles in the United States, or U.S. GAAP. All references herein to “dollars” or “$” are to United States dollars, and all references to “Shekels” or “NIS” are to New Israeli Shekels.

PART I.

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data are derived from our audited consolidated financial statements which have been prepared in accordance with U.S. GAAP. The selected consolidated financial data as of December 31, 2015 and 2014 and for the years ended December 31, 2015, 2014 and 2013 have been derived from our audited consolidated financial statements and notes thereto included elsewhere in this annual report. The selected consolidated financial data as of December 31, 2013, 2012 and 2011 and for the years ended December 31, 2012 and 2011 have been derived from audited consolidated financial statements not included in this annual report. The selected consolidated financial data set forth below should be read in conjunction with and are qualified by reference to “Item 5. Operating and Financial Review and Prospects” and our consolidated financial statements and notes thereto included elsewhere in this annual report.

Selected Financial Data

	Year ended December 31,				
	2011	2012	2013	2014	2015
	(US$ in thousands, except share and per share data)				
Consolidated Statement of Operations Data					
Revenues	$-	$242	$3,549	$12,367	$9,277
Cost of revenues	-	201	2,509	3,344	1,633
Total operating expenses (1)	11,979	13,583	18,083	21,360	28,562
Operating loss	(11,979)	(13,542)	(17,043)	(12,337)	(20,918)
Financial and other income (expenses), net	(25)	(86)	3,460	1,758	1,145
Equity loss	-	-	-	(155)	-
Losses before taxes on income	(12,004)	(13,628)	(13,583)	(10,734)	(19,773)
Taxes on income	-	-	(500)	(360)	(390)
Net loss	(12,004)	(13,628)	(14,083)	(11,094)	(20,163)
Realized and unrealized gain (loss) from investment in marketable securities and from foreign currency derivative contracts	(2,141)	1,103	(739)	(3,406)	(801)
Total comprehensive loss	(14,145)	(12,525)	(14,822)	(14,500)	(20,964)
Basic net loss per share	$(0.35)	$(0.38)	$(0.36)	$(0.23)	$(0.40)

Weighted average number of ordinary shares used in computing basic net loss per share	34,276,697	35,844,496	38,869,438	47,808,855	50,437,040
Diluted net loss per share	$(0.35)	$(0.38)	$(0.36)	$(0.26)	$(0.40)
Weighted average number of ordinary shares used in computing diluted net loss per share	34,276,697	36,249,262	38,869,438	48,387,063	50,437,040

(1) Includes stock based compensation – see Note 9 to our 2015 consolidated financial statements.

	As of December 31,				
	2011	2012	2013	2014	2015
	(US$ in thousands)				
Consolidated Balance Sheet Data					
Cash and cash equivalents, short-term bank deposits and restricted cash	$22,463	$19,685	$46,920	$73,328	$81,421
Trade receivable	-	-	-	-	7,800
Investment in marketable securities	4,093	5,196	4,565	1,054	426
Long-term bank deposits	-	-	-	35,026	-
Total assets	29,081	28,909	56,711	114,986	99,307
Deferred Revenues	-	-	6,772	1,789	312
Research and development funding arrangements and others	6,434	7,872	13,189	421	-
Accumulated deficit	(180,491)	(194,119)	(208,202)	(219,296)	(239,459)
Total shareholders' equity	$19,581	$17,672	$31,888	$106,116	$89,897

For additional financial information, please see "Item 5. Operating and Financial Review and Prospects – A. Operating Results,"

B. CAPITALIZATION AND INDEBTEDNESS

Not applicable.

C. REASONS FOR THE OFFER AND USE OF PROCEEDS

Not applicable.

D. RISK FACTORS

Many factors could affect our financial condition, cash flows and results of operations. We are subject to various risks including all the risks which are inherent in pharmaceutical discovery and development and those risks resulting from changing economic, political, social, industry, business and financial conditions in Israel and the major market countries. If we do not successfully, or cannot, address the risks to which we are subject, we could experience a material adverse effect on our business, results of operations and financial condition, which could include the need to limit or even discontinue our business operations, and accordingly our share price, may decline. We can give no assurance that we will successfully address any of these risks. The principal risks we face are described below.

Risks Related to our Business, Financial Results and Financing Needs

We cannot provide assurance that our business model will succeed in generating substantial revenues.

Our business model is primarily based on expected future revenues in the form of fees, research revenues, milestone payments, royalties on product sales and other revenue sharing payments from commercialization of products by third parties based on target candidates and/or their related product candidates discovered by us and licensed to such third parties pursuant to various forms of collaborations. In 2010, we began to focus our discovery efforts primarily on the prediction and selection of novel drug target candidates in specific areas of high interest in both oncology and immunology, and in particular, immune checkpoint candidates. The resulting predicted novel target candidates then undergo initial target validation studies and, in selected cases, are advanced to therapeutic product candidate discovery and early development (our "Pipeline Program") prior to proposed licensing or other forms of third party collaborations. To date, third party collaborations have only been entered into at early validation or pre-clinical stages which have an inherent risk of high failure rate. The inability to derive adequate revenues from our business model would materially harm our business, financial condition and results of operations and could result in the need to limit or even discontinue our business operations.

We have a history of losses, we expect to incur future losses and we may never achieve or sustain profitability.

As of December 31, 2015, we had an accumulated deficit of approximately $239.5 million and had incurred net losses of approximately $14.1 million in 2013, approximately $11.1 million in 2014 and approximately $20.2 million in 2015, in large part due to the expenditures related to the long-term establishment and continuing enhancement of our predictive discovery infrastructure, and more recently expenditures associated with our Pipeline Program. In addition, we expect to continue to incur net losses in the future due to the costs and expenses, now primarily associated with our Pipeline Program activities, including significantly increasing our activities in the United States, and to a lesser degree during the next few years, the development, validation and integration of additional discovery platforms. To date, we have entered into only one commercial arrangement with respect to our Pipeline Program candidates under which to date we have received, or are eligible to receive, a total amount of $25 million. Otherwise, we have received only minimal revenues from limited commercialization efforts with respect to discoveries made during our infrastructure

building period. We cannot be certain that we will receive additional revenues under our existing collaborations or enter into additional arrangements for our Pipeline Program candidates or other discoveries or capabilities, or that such additional arrangements will provide sufficient revenues to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability.

We may need to raise additional funds in the future, and if we are unable to raise such additional funds, we may need to curtail or cease operations. To the extent any such funding is based on the sale of equity, our existing shareholders would experience dilution of their shareholdings.

We believe that our existing cash and cash equivalents and short-term bank deposits will be sufficient to fund our current level of operations for at least the next 24-30 months, without considering the possible receipt of any additional funds, such as proceeds from existing or additional licensing and/or commercialization agreements, or from financings. However, we cannot predict with any degree of certainty when, or even if, we will achieve profitability and therefore may need additional funds to continue financing our discovery, validation, development and commercialization activities. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current and future operating plans.

Additional funds, including proceeds from commercialization agreements, or from other financings, may not be available to us when needed, on acceptable terms, or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our existing shareholders. For example, if we raise additional funds by issuing equity securities, our existing shareholders would experience dilution of their shareholdings. Debt financing, if available, may involve restrictive covenants that could limit our flexibility in conducting future business activities. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborators or others that may require us to enter into arrangements on terms that would otherwise not be acceptable to us. Any failure to raise funds when needed would materially harm our business, financial condition and results of operations.

We are currently pursuing our business model primarily in the fields of oncology and immunology, with a primary focus on immuno-oncology, and this limitation may not yield sufficient revenues to support our increasing level of activities.

Following establishment and validation of a sufficiently integrated infrastructure of our individual predictive discovery capabilities, we initiated our Pipeline Program to predict and select novel drug target candidates in specific areas of high interest in both oncology and immunology, with a primary focus on immuno-oncology. To date, we have entered into only one commercial arrangement, with Bayer Pharma AG (“Bayer”), with respect to two Pipeline Program drug target candidates (the “Bayer Collaboration”), under which to date we have received, or are eligible to receive, a total amount of $25 million. We cannot be certain this current focus on our discovery, research and development efforts to the fields of oncology and immunology, with a more specific focus on immuno-oncology, along with our decision to advance selected programs at our own expense, will generate a stable or significant revenue stream. The inability to derive adequate revenues within our field of focus would materially harm our business, financial condition and results of operations and could result in the need to limit or even discontinue our business operations.

Our Pipeline Program will require additional resources that may not be available.

In 2010 we initiated our Pipeline Program pursuant to which we are both (i) substantially increasing the number of predicted and selected drug target candidates being evaluated by us, and (ii) taking certain drug target candidates or Fc fusions based on such beyond their initial validation stage into disease animal model studies, therapeutic monoclonal antibody (“mAb”) discovery and evaluation and in selected cases, preclinical development of therapeutic product candidates and possibly their clinical evaluation. This may result in multiple drug target candidates or therapeutic product candidates reaching more costly stages of research and development in parallel. If we are not able to secure the funding or the capabilities required for such expanded amount and type of activities, we may be required to abandon, postpone, or attempt to license out certain drug target candidates or therapeutic product candidates at an earlier than anticipated stage, which may result in a substantial reduction in the potential returns from the Pipeline Program, or even result in the inability to have some or all of such therapeutic product candidates further developed towards potential commercialization.

We operate in a rapidly developing field and will be required to allocate substantial additional funds in the future to our research activities.

Our discovery capabilities rely on a proprietary integrated approach of predictive models, algorithms and other computational tools incorporating proprietary knowledge of key biological phenomena. Life science today is a rapidly changing field with substantial research being undertaken on a worldwide basis by both academia and industry. In order to maintain our competitive position in predictive discovery, we must continue to allocate resources to broadening and deepening our scientific infrastructure. Any inability to allocate such resources when needed could materially harm our future business, financial condition and results of operations.

We have a limited operating history with respect to the commercialization aspects of our business model upon which investors can base an investment decision or upon which to predict future revenues.

Our ability to generate revenues from collaboration and licensing activities for current and future drug target candidates and therapeutic product candidates based on these discoveries, primarily in the form of fees, research revenues, milestone payments, royalties and other revenue sharing payments has had limited success to date. In 2013, we entered into the Bayer Collaboration, our first collaboration with respect to two of our Pipeline Program drug target candidates, under which we have received, or are eligible to receive, to date a total amount of $25 million, and have received only minimal revenues from our earlier collaborations based on discoveries made during the building of our predictive discovery approach. We recognized $9.3 million in revenue in 2015, $12.4 million in revenue in 2014, and $3.5 million in revenue in 2013, approximately 98% of which related to the Bayer Collaboration. Furthermore, only in 2010 did we implement our Pipeline Program pursuant to which we are currently advancing certain therapeutic product candidates past disease animal model proof of concept or other validation studies. We therefore have very limited experience with respect to the financial terms that may be available for our candidates at later stages of validation and development, and financial terms for agreements by other companies, to the degree disclosed, vary greatly. Accordingly, our operating history with respect to the commercialization aspects of our business model provides a limited basis to assess our ability to generate significant fees, research revenues, milestone payments, royalties or other revenue sharing payments from the licensing, development and anticipated future commercialization of product candidates based on our existing and future target discoveries.

Risks Related to our Discovery and Development Activities

Our predictive discovery activities are focused on novel drug target candidates and our therapeutic product candidates are based on Compugen discovered targets.

While we believe that our novel target programs represent a compelling and unique opportunity to generate first-in-class therapeutic products, they require significant investment in the research and validation of the drug target candidate and its respective therapeutic product candidate. The lack of sufficient published scientific body of evidence to support the potential of our novel drug targets to serve as therapeutic target opportunities, increases the risk of failure. Although Compugen has built the infrastructure required to translate its novel targets into therapeutic antibody programs, we cannot be assured that our investment in such target programs will result in validated drug targets, or that we will realize success in product development or our ability to commercialize such opportunities and generate revenues.

Major pharmaceutical companies might be hesitant to pursue development programs based on novel targets lacking robust experimental validation results particularly those discovered through computational predictive discovery approach.

There is a growing recognition of the need for new drug targets generating new treatment options for non-responsive patients, particularly in areas where biologics have become more accessible to develop, as compared with small molecules. Our business model strategy seeks to combine early stage collaborations (where the novel target is the subject of the partnership) and later stage collaborations (where the lead antibody or clinical therapeutic product candidate against such novel target is the subject of the partnership). Our involvement in early stage collaborations, as opposed to the more common lead antibody, or product, based collaborations, generates challenges inherent to such target based collaborations and not present in more traditional product based collaborations. In addition, although we have had some success in the demonstration of our predictive discovery capabilities regarding novel drug target candidates, major pharmaceutical companies may be hesitant to enter into early stage collaborations based on novel targets discovered by computer, as opposed to drug targets with significant published experimental validation, or even targets validated in human clinical trials or being marketed. Therefore, we cannot assure that our strategy to enter into commercialization arrangements for our early stage novel targets will be successful.

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We are focusing our therapeutic development activities on mAb drug target candidates, and to a lesser degree, Fc fusion protein product candidates, for uses in oncology and immunology, based on Compugen discovered targets. If we fail to continue to discover and develop drug target candidates of industry interest in these fields, or to discover promising therapeutic mAbs against them, our business will likely be materially harmed.

Since late 2010 we have chosen to focus our Pipeline Program therapeutic discovery and development activities on mAb therapeutics and Fc fusion proteins based on Compugen discovered drug target candidates to address unmet needs in the areas of oncology and immunology, with the main focus on immuno-oncology and, to a lesser extent, autoimmune and inflammatory conditions. Based on this, we selected immune checkpoints as the objective for our first focused discovery program utilizing our broadly applicable predictive discovery infrastructure, and more recently undertook our second focused program aimed at discovery of targets for antibody-drug-conjugate (ADC) therapy. A result of our decision in 2010 to focus this way is that we are not undertaking internal discovery and development in other areas, including those where we previously demonstrated discovery capabilities, such as diagnostic products (other than biomarker discovery for selected internal checkpoint programs) and peptide based drugs, and presently intend to pursue such opportunities only in collaboration with third parties. With respect to checkpoint proteins, although there have been positive clinical results reported by others with respect to a number of products based on certain checkpoint proteins, resulting in substantial industry, academic and medical interest, with some products gaining FDA approval based on this positive data, there can be no assurance that our immune checkpoint target candidates, which currently are the basis for the majority of therapeutic product candidates in our Pipeline Program, will provide similar clinical advantages or interest, that no long term adverse effects will be seen, or that a different class of targets will not be discovered with comparable or superior attributes. In the event of any of these occurrences, the actual and/or perceived value of a substantial portion of our Pipeline Program would likely be reduced in which case our business may be harmed. Additionally, although certain of our initial candidates based on Compugen discovered immune checkpoint target candidates are generating interest from potential partners, to date we have signed only one collaboration involving two such discoveries and all our target candidates are at early stages of research and development. There is no assurance that we will be able to consummate additional collaborations or agreements on reasonable terms, if at all. In addition, if we fail to continue to discover drug target candidates of industry interest in our fields of focus, or to pursue validation and development efforts in our Pipeline Program on the most promising discoveries, our business will likely be materially harmed. There are many risks associated with this decision of focusing on these areas that include, among others:

- not utilizing all of our target discovery capabilities;
- choosing therapeutic areas with a very high degree of competition;
- choosing therapeutic areas of great complexity and with very high failure rates in product development;
- failing to validate the multiple novel drug target candidates we have discovered in our chosen therapeutics areas;
- having insufficient relevant knowledge in our chosen therapeutic areas to select the right unmet medical needs, or novel target candidates, or to timely, properly and efficiently select the appropriate mAb or Fc fusion candidates for further development as therapeutic product candidates, or to timely, properly or efficiently further them in development; and
- the inherent risk of high program failure rate in early stage therapeutic development.

In each case, our failure could be due to lack of experience, delays in our internal research programs or applying the wrong criteria or experimental systems and procedures, or unanticipated scientific issues, with the possible result that no candidates result in licensed or marketable products in these fields. If any of these risks should materialize, our

business, financial condition and results of operations would be materially harmed.

Our predictive discovery capabilities remain unproven with respect to yielding novel targets which can serve as the basis for marketable therapeutic products. If in further development and clinical evaluation of such resulting therapeutic candidates, all, or a larger percentage than typically seen in industry experience, of our product candidates fail to prove sufficiently safe and effective for regulatory approval and marketing, our business will be significantly harmed.

Our in silico (by computer) predictive approach to drug target discovery remains unproven with respect to yielding novel targets which can serve as the basis for marketable therapeutic products, and to date, our validation efforts for our initial targets and product candidates have been limited to in vitro testing and in vivo testing using animal disease models. These discovery capabilities, which are designed to predict and select novel drug target candidates in many different therapeutic areas of interest, rely on the modeling, by our scientists, of complex biological processes, both physiological and pathological. This modeling is partial and may prove insufficient to result in true predictions of the biological processes as they occur naturally. If in further development and clinical evaluation, all, or a larger percentage than typically seen in industry experience, of our therapeutic product candidates based on our novel drug targets fail to prove sufficiently safe and efficacious for regulatory approval and marketing, our business will be significantly harmed.

Our in silico predictive approach to target discovery typically results in a significant number of putative discoveries of interest with each discovery program. If we or our partners fail to select the right drug target candidates to validate and/or progress in the therapeutic development, due to either lack of experience or applying the wrong criteria or experimental methodology, the selected target candidates may never result in marketable therapeutic products and our business, financial condition and results of operations will be materially harmed.

Our in silico predictive approach to drug target discovery typically results in a significant number of putative discoveries of interest with each discovery program. Following each such discovery run, we assess which of such putative discoveries to move forward with initiation of validation based on various available scientific and business criteria, which may or may not be sufficient, and this assessment continues on an on-going basis. In addition, since our research and development resources are limited we are able to progress with only a fraction of our discoveries in parallel. If at any stage in such assessment, we or our partners fail to select the right drug target candidates to validate and/or progress in the therapeutic development, due to either lack of experience or applying the wrong criteria or experimental methodology, the selected candidates may never result in licensable targets or marketable products, and our business, financial condition and results of operations may be materially harmed.

The large number of drug target candidates in our Pipeline Program may dilute the required resources on each individual candidate and thus result in significant delays.

Our predictive in-silico methodology results in a large number of drug target candidates entering our Pipeline Program. Prosecuting multiple drug target candidates limits the resources available to each individual target candidate and might create delays or premature program prioritization. If such delays or premature program prioritization become significant this can make the resulting therapeutic product candidates less competitive or even obsolete as competing products advance or significantly reduce their value due to shorter patent term protection. Therefore, such delays may significantly harm these product candidates and our business.

If either the predictive discovery approach in general, or our “first-in class biologics for key medical needs” approach, does not prove to be successful, our business will be significantly harmed.

Our method of discovering novel drug target candidates involves first selecting either on our own or with a partner company an unmet key medical need where we believe our predictive capabilities would be relevant, or could be modified to be relevant. In this “first-in class biologics for key medical needs” approach, our goal is to harness all of our relevant predictive discovery capabilities in order to identify attractive novel drug targets for therapeutically

addressing the specific medical need of interest. Although our “first-in class biologics for key medical needs” approach has resulted in the discovery of a number of novel drug target candidates in several areas of significant industry interest, all of these drug target candidates and related therapeutic product candidates are in very early stages of research and development. Therefore, we cannot predict whether this “first-in class biologics for key medical needs” approach will continue to yield drug target candidates or that any of our existing discoveries or future discoveries will be suitable for the successful development of therapeutic products and that these will be first-in-class. If either the predictive discovery approach in general does not prove to be successful, or this “first-in class biologics for key medical needs” approach does not lead to successful therapeutic product candidates, our business will be significantly harmed.

Our focus on the Pipeline Program has resulted in a substantial increase in activities, certain of which we will undertake for the first time and may result in therapeutic product candidate failures, or fewer therapeutic product candidates being available for commercialization.

Until recently, our in vitro and in vivo validation studies concluded with the drug target candidate expression profile and/or functional analysis. Upon completion of such activities, or earlier, we initiated our efforts to enter into collaborations for such drug target candidates. This is at an earlier stage than is typical for licensing in the pharmaceutical industry. Pursuant to the Pipeline Program initiated in 2010, and with the increase in our R&D activities, we are both conducting validation studies and advancing target candidates in parallel, and intend to advance a number of therapeutic product candidates against such targets towards pre-clinical activities, with the possibility of some of these candidates being selected for future clinical evaluation. The decision to advance certain therapeutic product candidates further requires us to undertake certain activities for the first time and may result in product candidate failures either due to our lack of expertise, unsupportive findings, or lack of an appropriate technology, or due to the inherent risk of failure with respect to such activities. Furthermore, due to our limited resources, we must choose which Pipeline Program candidates to advance further in therapeutic product candidate early stage development, including possible clinical development in the future. This could result in fewer drug target candidates being available for commercialization, due to our available resources being insufficient to further advance all programs. In addition, if we fail to select the right drug target candidates or therapeutic product candidates to advance further, due to either lack of experience or applying wrong criteria or experimental methodology, the selected drug target candidates may never result in a licensable or marketable product. If any of these risks materialize, our business, financial condition and results of operations may be materially harmed.

We have limited experience in the development of therapeutic product candidates.

Our experience in the development of therapeutic product candidates is very limited. In order to successfully develop and commercialize therapeutic products, we must either access such expertise via collaborations or service providers, and/or continue to enhance and improve our internal expertise, capabilities and facilities. We may not be able to hire the scientists with the required expertise in a timely manner, if at all, and/or engage any or all of the service providers or other experts that we need in order to do so. If we fail to have available, at the appropriate times, the required experience and expertise for the further development and commercialization of our therapeutic product candidates, we may be unsuccessful in these activities, or these activities may be significantly delayed and as a result our business would be materially harmed.

Our establishment of our own therapeutic mAb research and development capabilities contains a number of risks.

In 2012, we announced that we had established our own therapeutic mAb development capabilities in our U.S. based, wholly owned subsidiary, Compugen USA, Inc., in order to discover and develop mAb therapeutics against the drug target candidates that we discovered. The establishment of such in-house capabilities contains a number of risks, including, without limitation, the need for additional resources and funding to maintain such capabilities or to acquire additional technologies, and the need to identify additional qualified employees and consultants in order to further advance these capabilities. Furthermore, although the scientists we have hired have prior experience with other organizations in the field of therapeutic mAb research and development, we have limited experience as a company in this field. Therefore, as a result, if we are unsuccessful in any of these required undertakings, our business could be materially harmed.

There are risks that are inherent in the development and commercialization of therapeutic products, and if these risks materialize, our business and financial results may be materially harmed.

We and our collaborators face a number of risks of failure that are inherent in the process of developing and commercializing novel therapeutic products. These risks, which typically result in very high failure rates even for

successful biopharma companies, include, among others, the possibility that:

- our drug target candidates will prove to be inappropriate targets for mAb therapeutics;
- our therapeutic product candidates will fail to progress to preclinical studies or clinical trials;
- our early stage commercialization efforts may provoke competition by potential partners;

- our early stage collaborations may face internal competition by our partners within their own organizations;
- our therapeutic product candidates will be found to be therapeutically ineffective;
- our therapeutic product candidates will be found to be toxic or to have other unacceptable side effects;
- our therapeutic product candidates will be inferior to or not show added value compared to competing products;
- we or our collaborators will fail to receive required regulatory approvals;
- we will not be able to generate differentiation for our therapeutic product candidates;
- we or our collaborators will fail to manufacture our therapeutic product candidates in the quantity or quality needed for preclinical studies or clinical trials on a large scale and in a cost effective manner;
- the commercialization of our therapeutic product candidates or our drug target candidates may infringe third party intellectual property rights;
- the development, marketing or sale of our therapeutic product candidates will fail because of our inability or failure to protect or maintain our own intellectual property rights;
- once a product is launched on the market, there will be little or no demand for it for a number of possible reasons, including lack of acceptance by the medical community or by patients, lack of or insufficient coverage and payment by third party payors, inefficient marketing and sales activities or as a result of there being more attractive, less risky or less expensive, products available for the same use; and
- the product will be withdrawn from the market, or sales limited due to side effects observed in clinical practice.

If one or more of these risks or any similar risks should materialize, our business and financial results may be materially harmed.

Risks Related to Development, Manufacturing, Clinical Trials and Government Regulation

We or our collaborators may be unable to obtain regulatory approval for any product that we or a collaborator may develop.

Any therapeutic product that we or our collaborators may attempt to develop, manufacture or market in the United States will be subject to extensive governmental regulations, including those relating to development, preclinical testing, performance of clinical trials, manufacturing and post-approval commercialization. Preclinical testing, clinical trials and manufacturing, among other activities, will be subjected to an extensive review process before a new therapeutic product may be sold in the United States. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. The time required to obtain U.S. Food and Drug Administration, or FDA, approval, and any other approvals for therapeutic products is unpredictable but typically requires several years.

Any therapeutic product that we or our collaborators may wish to develop, manufacture or market in countries other than the United States will also be subject to numerous regulatory requirements governing the conduct of clinical trials, manufacturing and marketing, pricing and third-party reimbursement among other things in such countries. The foreign regulatory approval process includes all of the risks and uncertainties associated with FDA approval described

above as well as risks attributable to the satisfaction of local regulations in such foreign jurisdictions.

It is possible that none of the therapeutic products we or our collaborators may develop will obtain the approvals necessary for us or our collaborators to sell them either in the United States or any other country. Furthermore, approval by the FDA of a therapeutic product does not assure approval by regulatory authorities outside the United States or vice versa. Even if approval for a therapeutic product is obtained, such approval may be subject to limitations on the indicated uses or appropriate patient population that could result in a significantly reduced potential market size for the product.

If we or our collaborators fail to obtain the appropriate regulatory approvals necessary for us or our collaborators to sell our products, or if the approvals are more limited than those that we intend to seek, our business, financial condition and results of operations would be materially harmed.

It may be difficult to manufacture therapeutic products based on our technologies.

Our Pipeline Program is focused mainly on mAbs and, to a lesser extent, on Fc fusion protein therapeutics in the fields of oncology and immunology, with a primary focus on immuno-oncology, and such therapeutic types can be difficult to manufacture in the quantity and quality needed for preclinical, clinical and commercial use. The production of mAbs and protein therapeutics must be conducted pursuant to a well-controlled and reproducible process and the resulting product testing must conform to defined quality standards. Should it prove to be difficult to manufacture any therapeutics based on our technologies in sufficient quantities, meeting the required quality standards or in an economical manner to conduct clinical trials and to commercialize any approved therapeutic candidate, our business, financial condition and results of operations would be materially harmed.

If we or any of our collaborators, or third-party manufacturers, fail to comply with regulatory requirements, we or they could be subject to enforcement actions, which could affect the marketability of Compugen-discovered therapeutics and may significantly harm our financial status and/or reputation.

If we or any of our collaborators or third-party manufacturers with which we may enter into agreements in the future fail to comply with applicable federal, state or foreign laws or regulations, we or they could be subject to enforcement actions. These enforcement actions may include:

- warning letters;
- clinical trial holds;
- recalls, product seizures or medical product safety alerts;
- data lock, for failure to comply with applicable privacy and data security laws;
- restrictions on, or prohibitions against, marketing such tests or products;
- restrictions on importation of such tests or products;
- suspension of review or refusal to accept or approve new or pending applications;
- withdrawal of product approvals;
- injunctions;
- civil and criminal penalties and fines; or
- debarment or other exclusions from government programs.

If we or our collaborators become subject to such enforcement actions, these enforcement actions, could affect the ability to successfully develop, market and sell therapeutic products based on our discoveries and could significantly harm our financial status and/or reputation and lead to reduced acceptance of such products by the market.

If we do not comply with laws regulating the use of human tissues or other human biological samples or the conduct of experiments involving animals, our business could be adversely affected.

We use human tissue samples and other human biological samples and conduct experiments involving animals for the purpose of development and validation of our technologies, discoveries and product candidates. Our access to and use

of human tissue samples and other human biological samples and the conduct of experiments involving animals are subject to government regulation in the United States, Israel and elsewhere and may become subject to additional regulation. For example, the Israeli Ministry of Health requires, among other things compliance with the principles of the Helsinki Declaration, the Public Health Regulations (Clinical Trials in Human Subjects) 5740-1980, the Genetic Information Law, 5761-2000, the provisions of the Israel Ministry of Health Guidelines for Clinical Trials in Human Subjects and the provisions of the current Harmonized Tripartite Guideline for Good Clinical Practice. Our use of clinical data related to any tissue or other human biological samples must comply with applicable local, national and international privacy law. Our use of animal models for pre-clinical research must comply with the U.S. Animal Welfare Act, the United States Public Health Service Policy on Humane Care and Use of Laboratory Animals, and applicable state and local laws.Our failure, or the failure of our subcontractors or collaborators, to comply with these or similar regulations could negatively impact our business and results of operations.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research and development activities involve the use of hazardous materials and chemicals, and we maintain quantities of microbial agents, various flammable and toxic chemicals in our facilities. Although we believe our safety and other procedures for storing, handling and disposing these materials in our facilities comply with applicable governmental and local regulations and guidelines, the risk to our employees or others of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which may exceed our financial resources and may seriously harm our business. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials. We may be subject to liability and may be required to comply with new or existing laws and regulations regulating pharmaceuticals or be subject to substantial fines or penalties if we violate any of these laws or regulations.

Risks Related to Our Dependence on Third Parties

We depend significantly on third parties to carry out the research, development and commercialization of our therapeutic product candidates. If we are unable to maintain our existing agreements or to enter into additional agreements with such third parties in the future, our business will likely be materially harmed.

Our primary strategy for the further development and commercialization of products based on our drug target and therapeutic product candidates depends on third parties to carry out and/or finance, research, development and commercialization of such products, principally pharmaceutical, and biotechnology companies and other healthcare related organizations. To date, we have entered into one collaboration with Bayer with respect to two drug target candidates from our Pipeline Program and established a JV with Merck-Serono for the discovery and development of biomarkers for the prediction of drug-induced hepatotoxicity. None of the candidates subject to such agreements have advanced beyond the discovery and pre-clinical stages or beyond diagnostic biomarker development stage, and we cannot be sure that either of these agreements will result in the successful development or commercialization of any products. Further, we cannot provide assurance that we will succeed in identifying additional suitable parties or entering into any other additional agreements on satisfactory terms or at all for the discovery, research, development and/or commercialization of our drug target or therapeutic product candidates. If we are unable to identify such additional suitable parties or enter into new agreements on satisfactory terms, or at all, our business will likely be materially harmed.

Our dependence on collaboration agreements with third parties presents a number of risks, and if one or more of these risks materialize, our business may be materially harmed.

The risks that we face in connection with our existing collaborations, licenses and other business alliances as well as those that we may enter into in the future include, among others, the following:

- we may be unable to reach mutually agreeable terms and conditions with respect to potential new collaborations;
- we may be unable to comply or fully comply with our obligations under collaboration agreements into which we enter, and as a result, we may not generate royalties or milestone payments from such agreements, and our ability to enter into additional agreements may be harmed;
- our obligations under existing or future collaboration agreements may harm our ability to enter into additional collaboration agreements;
-

our collaborators have significant discretion in electing whether to pursue any of the planned activities and the manner in which it will be done, including the amount and nature of the resources to be devoted to the development and commercialization of our product candidates;

- our collaborators have significant discretion in terminating the collaborations for scientific, business or other reasons;

- if our collaborators breach or terminate an agreement with us, the development and commercialization of our therapeutic product candidates could be adversely affected because at such time we may not have sufficient financial or other resources or capabilities to successfully develop and commercialize these therapeutics on our own or find other partners;

- our collaborators may fail to design and implement appropriate preclinical and/or clinical trials;

- our collaborators may fail to manufacture our therapeutic product candidates needed for either clinical trials or for commercial purposes on a sufficiently large scale , in the required quality and/or in a cost effective manner;

- our collaborators may fail to develop and market products based on our discoveries due to various regulatory restrictions;

- our collaborators may fail to develop and market products based on our discoveries prior to the successful marketing of competing products by others or prior to expiry of the patents protecting such products;

- changes in a collaborator's business strategy may negatively affect its willingness or ability to complete its obligations under its arrangement or to continue with its collaboration with us;

- our collaborators may terminate the program or the agreement and then compete against us in the development or commercialization of similar therapeutics;

- ownership of the intellectual property generated under or incorporated in our collaborations may be disputed;

- our ownership of rights in any intellectual property or products that may result from our collaborations may depend on additional investment of money that we may not be able or willing to make;

- prospective collaborators may pursue alternative products or technologies, by internally developing them or by preferring those of our competitors;

- disagreements between us and our collaborators may lead to delays in, or termination of, the collaboration;

- our collaborators may fail to develop or commercialize successfully any products based on our novel targets or product candidates to which they have obtained rights from us;

- our early stage collaborations may face internal competition by our partners within their own organizations;

- prospective collaborators may hesitate to pursue collaborations on novel target candidates that lack robust validation to serve as a basis for the development of therapeutics; and

- our collaboration partners may be acquired by, acquire, or merge with, another company, and the resulting entity may have different priorities or competitive products to the collaboration product being developed previously by our partner.

If any of these risks should materialize, our business, financial condition and results of operations may be materially harmed.

To date we have entered into only one collaboration agreement with respect to our Pipeline Program drug target candidates, and this agreement with Bayer is subject to many risks. If such agreement is terminated by Bayer, particularly prior to our signing additional collaboration agreements, our business and financial condition may be materially harmed.

In August 2013, we entered into a Research and Development Collaboration and License Agreement with Bayer for the research, development, and commercialization of antibody-based therapeutics for cancer immunotherapy against

two novel, Compugen-discovered immune checkpoint regulators – CGEN 15001T and CGEN 15022. This is our first collaboration arrangement for any of our Pipeline Program candidates.

The collaboration with Bayer is subject to all of the risks as set forth above with respect to our dependence in general on collaboration agreements with third parties. In addition, since this is our first collaboration involving our Pipeline Program candidates, and specifically covering Compugen-discovered immune checkpoint target candidates, until such time as we have additional agreements, the effect of any event related to this collaboration will likely have a significantly greater effect on our business and financial condition than otherwise would be the case.

Bayer may terminate the agreement, at any time with or without cause either in whole or only with respect to one of the two programs, and in each case also on a product-by-product and/or country-by country basis, upon prior written notice. Upon any termination of the agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the continued development and commercialization of any products and or various payment and royalty obligations in the event of such continuation of the development and commercialization. If significant adverse unforeseen events occur in the Bayer collaboration or the agreement is terminated, in whole or in part, particularly prior to our signing additional collaboration agreements, our business and financial condition may be materially harmed.

Our reliance on third parties for the performance of key research, validation and development activities heightens the risks faced by our business.

We invest significant efforts and resources into outsourcing certain key functions with third parties, including certain research, validation and development activities, manufacturing operations, and others. We do not control the third parties to whom we outsource these functions, but we depend on them to undertake activities and provide results or materials, including the production of certain biological reagents, which may be significant to us. If these third parties fail to properly or timely perform these activities, or provide us with incorrect or incomplete results, or fail to produce and/or provide certain materials this could lead to significant delays in the program or even program failure, along with significant additional costs. In addition, should any of these third parties fail to comply with the applicable laws and regulations and/or research and development or manufacturing accepted standards in the course of their performance of services for us, there is a risk that we could be held responsible for such violations of law as well. Any such failures by third parties could have a material adverse effect on our business, financial condition or results of operations.

Moreover, we do not always independently verify the results obtained by such third parties and in some cases, rely upon the data provided by the third party. If we fail to identify and obtain accurate and quality services technologies and/or data from such third parties, or if the contractual demands of such third parties become unreasonable and we are not able to reach satisfactory agreements with such third parties, we may not be able to obtain the required services and/or technologies, in which event we may lose our investment in these services, fail to receive the expected benefits from our discoveries, and our validation and development capabilities or activities, may be significantly harmed or delayed.

Additionally we have entered into an agreement to obtain access to a highly diverse human phage display antibody library to generate antibodies against novel target candidates for our Pipeline Program. The current term of this agreement terminates in June 2016, unless we pay certain renewal fees. In addition, if we fail to comply with the provisions of this agreement, the third party from which we have obtained license to this library may terminate our rights to use the library, which could harm our business, financial condition or results of operations.

We have limited experience and capabilities in conducting, managing or sponsoring preclinical evaluation of therapeutic product candidates.

During 2010, we began to focus our discovery efforts primarily in the fields of oncology and immunology, and initiated the Pipeline Program to both substantially increase the number of drug target candidates in our validation pipeline and to increase the value of certain of our drug target candidates by advancing selected therapeutic product candidates to pre-clinical studies and in selected cases, possibly clinical evaluation. We have limited experience and capabilities in conducting, managing or sponsoring the work and efforts required beyond the proof of concept experimental validation stage towards preclinical evaluation, and by doing so we will need to rely on our consultants and third party service providers. If we fail to identify the right consultants or service providers, if the consultants or service providers fail in providing the required services or if we fail to take the necessary steps towards preclinical evaluation, for these or other reasons, our business may be harmed.

We have no experience in conducting or managing clinical trials for potential therapeutic products, and rely on third parties to conduct such trials on our behalf. If these third parties are not successful in carrying out their duties our development of potential products may be delayed.

We have no experience in conducting or managing the clinical trials necessary to obtain regulatory approvals for any product, and we intend to rely on our collaborators or third parties, such as contract research organizations, or CROs, medical institutions and clinical investigators to perform these functions. Our reliance on third parties for clinical development activities reduces our control over these activities. Third-party contractors may not complete activities on

schedule, or may not conduct clinical trials in accordance with regulatory requirements or our trial design. If these third parties do not successfully carry out their contractual duties or meet required performance standards or expected deadlines, we might be required to replace them, or the data that they provide could be rejected, all of which may result in a delay of the affected trial and additional program costs.

We rely on access to public and commercial databases to feed our discovery capabilities, including our individual discovery platforms. If we are denied access to these databases, if the quality of available information is poor, or if the quantity of the available information is insufficient, our operations and business may be harmed.

In the development, validation and continuing expansion and enhancement of our discovery platforms and other tools, as well as in connection with the resulting drug target and therapeutic product candidates, we rely on our ability to access and use public and commercially available databases. The quality of our platforms, tools and discoveries is in part dependent on the quality and quantity of the data in these databases. If we are denied access to these databases, if we are granted access to such databases on terms which are not commercially reasonable, if the quality of data available from those databases is poor, or if the quantity of the available information is insufficient, each of which has occurred in the past, our business and our results of operations may be materially harmed.

We rely on access to high-quality biological samples supported by detailed clinical records to conduct parts of our discovery and validation activities. If we fail to identify and purchase or otherwise obtain such samples, if the quality of available biological samples is poor, or if the quantity of the available biological samples is insufficient, which has occurred in the past, our discovery and validation capabilities may be harmed.

In carrying out our discovery and validation of drug target candidates, we rely on our ability to access and use commercially available biological samples. The quality of our discoveries is in part dependent on the quality and quantity of available biological samples. If we fail to identify and purchase or otherwise obtain such samples for any reason, if the quality of available biological samples is poor, if the samples have not been obtained and made available for secondary use in accordance with applicable law, or if the quantity of the available biological samples is insufficient, which has occurred in the past, our discovery and validation capabilities may be harmed.

Risks Related to Competition and Commercialization

Our business model is at an early stage of implementation and to date has not yielded significant revenues.

The success of our business model relies on providing to third parties for commercialization, through licensing agreements and other forms of collaboration, therapeutic product candidates at various stages of research and development, or the rights to develop such candidates, in each case based on our discovered novel drug target candidates. Additionally, our business model includes research and discovery collaborations aimed at harnessing our infrastructure capabilities towards the partners' discovery needs. Our objective is that these collaborations, anticipated to be primarily with pharmaceutical and biotechnology companies, will be "product oriented", with us having the right to receive fees, research revenues, milestones, royalties and other revenue-sharing payments from such products commercialized by, or on behalf of, such third party. Our commercialization efforts are at an early stage of implementation. To date, we have entered into the Bayer Collaboration with respect to two drug target candidates from our Pipeline Program and established a joint venture with Merck-Serono ("Neviah") for the discovery and development of biomarkers for the prediction of drug-induced hepatotoxicity. In addition, in the past we entered into a number of other small collaboration agreements, none of which provided significant revenues.

There can be no assurance that any current or future agreements based on our discoveries and product candidates based on such discoveries will be successful and thus provide significant revenues to our Company, nor can there be any assurance that we will be able to enter into additional future agreements. If we are unable to achieve success, primarily by entering into additional license agreements or other collaboration arrangements related to our discoveries, our business will be materially harmed.

In addition, our internal programs are in the target discovery, research and validation stage, and/or in the early therapeutic product preclinical stage. The validation and other data generated to date may not be sufficient for prospective collaborators, and furthermore the drug target candidate or prospective therapeutic product candidate may

not fit their strategy. These companies may hesitate or require more data before considering a significant collaboration. We are therefore dependent on the fit of our programs to pharma strategy and, there can be no assurance that we will be able to identify additional partners interested in our programs at their current stages of research and development. This may adversely affect our ability to enter into additional agreements for the research, development and commercialization of our therapeutic product candidates, and as a result may harm our business.

Furthermore, industry trend towards drug combinations in the field of cancer immunotherapy, mainly for immune modulating agents such as drugs targeting immune checkpoints, may result in a situation under which our therapeutic product candidates will serve in a combination product and may therefore be entitled to only a fraction of the anticipated product revenues. This trend may adversely affect any revenues we may be entitled to receive and as a result may harm our business.

The agreement cycle for potential collaborations is complex and lengthy and as a result, we may expend substantial funds and management resources with no assurance of success.

In general, each potential license agreement or other form of collaboration we may enter into will require negotiating with our potential partner a large number of scientific, legal and business terms and conditions that can vary significantly in each instance due to the specific drug target candidate or the therapeutic product candidate or candidates involved, and the potential partner's licensing, development and business operations and strategy. The accommodation of these requirements mandates a thorough consideration of both the scientific and business aspects of each transaction. Furthermore, the diversity and wide applicability of our discovery capabilities and our therapeutic product candidates, together with the fact that we are mainly located in Israel, adds additional levels of complexity to our business development efforts. As a result, the process of preparing and negotiating our licensing and other agreements may take more than 12 months and will require the input and substantial time and effort of our key scientific and management personnel. Accordingly, we will need to expend substantial funds and substantial key personnel time and effort into these business development activities with no assurance of successfully entering into agreements with potential collaborators and this could harm our business.

The trend towards consolidation in the pharmaceutical, diagnostic and biotechnology industries may adversely affect us.

There is a trend towards consolidation in the pharmaceutical, diagnostic and biotechnology industries. Although this consolidation trend is diminishing, it may still result in the remaining companies having greater financial resources and discovery and technological capabilities, thus intensifying competition in these industries. This trend may also result in fewer potential collaborators or licensees for our therapeutic and diagnostic product candidates. Also, if a consolidating company is already doing business with our competitors, we may lose existing or potential licensees or collaborators as a result of such consolidation. In addition, if a consolidating company is already doing business with us, we may lose the interest of the consolidating parties in our discovery capabilities or individual discoveries as a result of a modified strategy and new priorities of such consolidated entity. This trend may adversely affect our ability to enter into agreements for the development and commercialization of our therapeutic product candidates, and as a result may harm our business.

The biotechnology and pharmaceutical industries are highly competitive, and we may be unable to compete effectively.

The biotechnology and pharmaceutical industries in general, and the immune-oncology field in particular, are highly competitive. Numerous entities in the United States, Europe and elsewhere compete with our efforts to discover, validate, develop and partner with licensees and/or collaborators to commercialize drug target and therapeutic products or other product candidates. Our competitors include pharmaceutical and biotechnology companies, academic and research institutions and governmental and other publicly funded agencies. We face, and expect to continue to face, competition from these entities to the extent they develop products that have a function similar or identical to the function of our therapeutic product candidates in the fields of oncology and immunology that may attract our potential collaborators or that may reach the market sooner. We also face, and expect to continue to face, competition from entities that seek to develop technologies that enable the discovery of novel targets, antibodies and Fc fusion proteins in the fields of oncology and immunology. Many of our competitors have one or more of the following:

- much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization process;

- more extensive experience in preclinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing and marketing diagnostics therapeutics;

- more extensive experience in oncology, immunology and immuno-oncology and in the fields of mAb therapy and fusion protein therapeutics;

- products that have been approved or are in late stages of development; reduced reliance on collaborations or partnerships with third parties in order to further develop and commercialize competitive therapeutic products; and

- collaborative arrangements in our target markets with leading companies and research institutions.

Since we are a small company with limited human and financial resources, we are not able to work with a large number of collaborators in parallel and/or advance a large number of drug target or therapeutic product candidates in parallel. Our competitors may develop or commercialize products with significant advantages over any therapeutic products we, our collaborators or third-party licensees may develop. They may also obtain patents and other intellectual property rights before us, or broader than ours, and thereby prevent us from pursuing the development and commercialization of our discoveries. They may also develop products faster than us and therefore limit our market share. Our competitors may therefore be more successful in developing and/or commercializing products than we, our collaborators, or third party licensees are, which could adversely affect our competitive position and business. If we are unable to compete successfully against existing or potential competitors, our financial results and business would be materially harmed.

Changes in healthcare policy could increase our expenses, decrease our revenues and impact sales of, and reimbursement for, our products.

Our ability to commercialize our future therapeutic product candidates successfully, alone or with collaborators, will depend in part on the extent to which coverage and reimbursement for these product candidates will be available from government health programs, such as Medicare and Medicaid in the United States, private health insurers and other third-party payors. At present, significant changes in healthcare policy, in particular the continuing efforts of the U.S. and other governments, insurance companies, managed care organizations and other payors to contain or reduce health care costs are being discussed, considered and proposed.

For example, in the United States, there have been several initiatives implemented to achieve these aims. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, the “ACA”), substantially changes the way health care is financed by both governmental and private insurers. The ACA contains a number of provisions that are expected to impact our business and operations, including those governing enrollment in federal healthcare programs and reimbursement changes which will impact existing government healthcare programs and will result in the development of new programs.

In addition to the ACA, there will continue to be proposals by legislators at both the federal and state levels, regulators and third-party payors to keep these costs down. In general, it is too early to predict specifically what effect these acts and their implementation or any future healthcare reform legislation or policies in the United States or other countries will have on our business, including our ability to set prices for our product candidates which we believe are fair, and therefore our ability to generate revenues and achieve and maintain profitability. Yet, current and future healthcare reform legislation and policies could have a material adverse effect on our business and financial condition.

Risks Related to our Operations

Our operations including research and development are centralized at two sites without significant redundancies. Physical or environmental damages or other reasons making one or both sites non-operational may significantly affect our business.

Our company has two major sites, in Holon, Israel and South San Francisco. Damage to either or both of these sites due to natural calamities or other reasons can significantly disrupt our business, delay our business operations, jeopardize our ability to meet contractual obligations or patent prosecution deadlines and result in significant harm to

our business.

We may be unable to hire or retain key personnel or sufficiently qualified employees, in which case our business may be harmed.

Our business is highly dependent upon the continued services of our senior management and key scientific and technical personnel. While members of our senior management and other key personnel have entered into employment or consulting agreements and non-competition and non-disclosure agreements, they can terminate their employment agreements with us at any time without cause. We cannot be sure that these key personnel and others will not leave us or compete with us, which could harm our business activities and operations. It is difficult to find suitable and highly qualified personnel in certain aspects of our industry, mainly in the field of immuno-oncology.

It can also be difficult for us to find employees with appropriate experience for our business. During the year 2015 we continued to increase our number of employees, and our plans to further increase our R&D budget and activities during the year 2016 will require increased efforts to attract the required personnel with the required expertise and experience. We require a multidisciplinary approach and some of our researchers require an understanding in both exact and biological sciences. In addition, we require experience in drug development and immuno-oncology, for which there is significant competition, mainly in the U.S.A., for highly qualified personnel in these fields. As a result, we may face higher than average employee turnover or challenges in hiring due to such competition. Our business may be harmed if we are unable to retain our key personnel, or to attract, integrate or retain other highly qualified personnel in the future.

We may be unable to safeguard the integrity, security and confidentiality of our data or third parties' data, and if we are unable to do so, our business may be harmed.

We rely heavily on the use and manipulation of large amounts of data and on the secure and continuous use of our internal computers, communication networks and software and hardware systems. We have implemented and maintain physical and software security measures to preserve and protect our computers and communication, hardware and software systems as well as our data and third parties' data. However, these methods may not fully protect us against fire, storm, flood, power loss, earthquakes, telecommunications failures, physical or software break-ins or similar events. In addition, these measures may not be sufficient to prevent unauthorized access, use or publication of such proprietary data. A party who is able to circumvent our security measures could misappropriate or destroy (partially or completely) proprietary information or cause interruptions in our operations. In addition, a party, including an employee or a contractor, who obtains unauthorized access to our proprietary data or breaches a confidentiality agreement with us could publish or transfer large portions or all of our proprietary data. Some of our proprietary data is maintained in secured cloud services that may also be subject to security breach, including by employees of the cloud services provider. Such publication of proprietary data could materially harm our intellectual property position, thereby seriously harming our competitive position. Such security breaches, if significant, could materially harm our operations and even cause our business to cease.

Risks Related to Intellectual Property.

We may not be able to obtain or maintain patent protection for our inventions and if we fail to do so, our business will likely be materially harmed.

We have applied for patents covering targets, therapeutic and diagnostic product candidates and their method of use, and the success of our business depends, to a large extent, on our ability to obtain and maintain such patents and any additional patents covering our future drug targets and product candidates. As of February 1, 2016 we had a total of 61 issued and allowed patents, of which 39 are U.S. patents, eight are Australian patents, four are Israeli patents, five are European patents, one is Canadian patent, one is New Zeeland patent and three are Japanese patents. Our issued patents expire between 2020 and 2029. We also have 137 pending patent applications, which as of February 1, 2016, included 28 patent applications that have been filed in the United States, 17 patent applications that have been filed in Europe, 23 patent applications that have been filed in Israel, 12 patent applications that have been filed in Australia, 9 patent applications that have been filed in Canada, 9 patent applications that have been filed in Japan, 5 patent applications that have been filed in India, 5 patent applications that have been filed in China, 3 patent applications that have been filed in Brazil, 3 patent applications that have been filed in Korea, 3 patent applications that have been filed in New Zealand, 3 patent applications that have been filed in the Russian Federation, 3 patent applications that have been filed in Singapore, 3 patent applications that have been filed in Mexico, 3 patent applications that have been filed in South Africa, 3 patent applications that have been filed in Hong Kong, two patent applications that have been filed in Egypt and three applications that have been filed under the Patent Cooperation Treaty for which we have not yet designated the countries of filing. We plan to continue to apply for patent protection for our drug target candidates, therapeutic and diagnostic inventions, but we cannot be sure that any of our patent applications will be accepted, or

that they will be accepted to the extent that we seek. Additionally, we file for patent protection in selected countries and not in all countries of the world. Therefore, we are exposed to competition in those countries in which we have no patent protection. Also, due to our early stage business model, we may be required to seek patent protection at a very early stage. This may cause us to file with insufficient supportive data, possibly making it difficult to obtain patents in jurisdictions that do not accept post filing evidence to support the claims, and thus enabling others to compete with us. This may also cause issuance of a patent at an earlier stage creating a shorter commercialization period under patent protection, possibly enabling others to compete with us. Delays in filing patents may preclude us from obtaining protection on some or all of our drug target candidates and product candidates due to others filing ahead of us. Patent applications filed before us, but yet unpublished may cause us to spend significant resources in areas that due to these previously filed patent we are not able to obtain patent protection or that the scope of protection is much narrower than contemplated.

The process of obtaining patents for inventions that cover our products is uncertain for a number of reasons, including but not limited to:

- in view of the multiple inventions that typically result from our predictive discovery methodologies, we need to accurately select those that we seek patent coverage for
- the patenting of inventions involves complex legal issues relating to intellectual property laws, prosecution and enforcement of patent claims across a number or patent jurisdictions, many of which have not yet been settled;
- legislative and judicial changes, or changes in the examination guidelines of governmental patent offices may negatively affect our ability to obtain patent claims to certain biologic molecules- and/or use of certain therapeutic targets;
- in view of the finite number of human proteins, we face competition from other biotechnology and pharmaceutical companies who have already sought patent protection relating to proteins and protein based products, as well as therapeutic and diagnostic antibodies or other modulators specifically binding these proteins, and their utility based discoveries that we may intend to develop and commercialize; such prior patents may negatively affect our ability to obtain patent claims on certain proteins antibody or other biologic modulators, or may hinder our ability to obtain sufficiently broad patent claims for our inventions, and/or may limit our freedom to operate;
- publication of gene and/or data on gene products by non-commercial and commercial entities may hinder our ability to obtain sufficiently broad patent claims for our inventions;
- even if we succeed in obtaining patent protection, such protection may not be sufficient to prevent third parties from circumventing our patent claims;
    - even if we succeed in obtaining patent protection, we may face freedom to operate (FTO) issues;
- even if we succeed in obtaining patent claims protecting or our inventions and product candidates, our patents could be subject to challenge and litigation by our competitors, and may be partially or wholly invalidated as a result of such legal/judicial challenges;
    - there are significant costs that may need to be incurred in registering and filing patents;
- our data may be insufficient to support our claims and/or may support others in strengthening their patents;
- seeking patent protection at an early stage may prevent us from providing comprehensive data supporting the patent claims and may prevent allowance of certain patent claims or limit the scope of patent claim coverage;
- we may not be able to supply sufficient data to support our claims, within the legally prescribed time following our initial filing in order to support our patent claims and this may harm our ability to get appropriate patent protection or protection at all; and
- our claims may be too broad and not have sufficient enablement, in which case such claims might be rejected by patent offices or invalidated in court.

The U.S. Supreme Court, or the Court, has also issued decisions for which the full impact is not yet understood. On June 13, 2013, in Association for Molecular Pathology v. Myriad Genetics, Inc. the Court held that claims to isolated genomic DNA were not patentable subject matter, but claims to complementary DNA (cDNA) molecules were patentable subject matter. The USPTO Examination Guidelines, first issued in March 2014 (with updated guidelines issued in December 2014 and July 2015), introduced new procedure for determining subject matter eligibility of claims post Myriad, and they include specific questions and factors that weigh against or for patent eligibility of other isolated natural products. However these rules are still in flux, as additional decisions of the Court and/or lower courts impact the USPTO Examination Guidelines, which are then adjusted accordingly. On March 20, 2012, in Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc., the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision has created uncertainty around the ability to patent certain biomarker-related method patents. In a 2014 decision rendered by the Court of Appeals for the Federal Circuit in Abbvie Deutschland v. Janssen Biotech and Centorcor Biologics, Fed. Cir. July 1, 2014, the jury found both Abbvie's patents on fully humanized antibodies to IL-12 invalid as failing the written description requirement. There are no clear rules regarding the number of species that must be disclosed to describe a genus claim, as this number necessarily changes with each invention, and it changes with progress in the field. Although it is well-settled that the written description requirement does not require actual reduction to practice of all of the representative species, a patentee must provide a clear correlation between common structural elements and function across the whole genus. These decisions have increased the uncertainty with regard to our ability to obtain patents in the future as well as the value of current and future patents, once obtained. Depending on decisions by the U.S. federal courts and the Patent Office, the interpretation of laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents, all of which could have a material adverse effect on our business.

We may also be affected by decisions regarding the patents of others, which may impact our ability to make, use, sell, license or otherwise engage in business for our own inventions, due to the possibility of patent infringement. For example, BMS (Bristol-Myers Squibb) and partners sued Merck & Co over alleged infringement of the BMS partner's patent for anti-PD-1 antibody treatment of metastatic melanoma. We do not know the outcome of this lawsuit nor how it will impact our own business.

If we do not succeed in obtaining patent protection for our inventions (should it be discoveries, drug targets candidates and product candidates) to the fullest extent for which we seek protection, or if we fail to select the best inventions to seek such protection, our business and financial results could be materially harmed.

We may not be able to protect our non-patented proprietary data, know-how, technologies or discoveries, and that may materially harm our business.

Aside from our patented information, we also rely on our proprietary know-how and trade secrets that we develop and that are not protectable or protected by patents. The protective measures that we employ may not provide adequate protection for our trade secrets and know-how. Our business collaborators, licensees, employees, advisers and consultants may disclose our proprietary know-how or trade secrets in violation of their obligations to us. We may not be able to meaningfully protect our rights in our proprietary know-how or trade secrets against such unauthorized disclosure and any consequent unauthorized publication. In addition, others may independently discover trade secrets and proprietary information, and in such cases we could not assert any trade secret rights against such party. 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.

If we are not able to adequately protect our proprietary know-how and trade secrets, competitors may be able to develop technologies and resulting discoveries and inventions that are the same or similar to our own discoveries and inventions. That could erode our competitive advantage and materially harm our business.

The existence of third party intellectual property rights may prevent us from developing our discoveries or require us to expend financial and other resources to be able to continue to do so.

In selecting a therapeutic product candidate or diagnostic product candidate for development, we take into account, among other considerations, the existence of third party intellectual property rights that may hinder our right to develop and commercialize that product candidate. The human genomic pool is finite. To our knowledge, third parties, including our competitors, have been filing wide patent applications covering an increasing portion of the human genomic pool and the proteins and peptides expressed therefrom. As a result of the existence of such third party intellectual property rights, we have been and may be further required to:

- forgo the research, development and commercialization of certain drug target candidates and product candidates that we discover, notwithstanding their promising scientific and commercial merits; or

- invest substantial management and financial resources to either challenge or in-license such third party intellectual property, and we cannot be sure that we will succeed in doing so on commercially reasonable terms, if at all.

We do not always have available to us, in a timely manner, information of the existence of third party intellectual property rights related to our own discoveries. The content of U.S. and other patent applications remains unavailable to the public for a period of approximately 18 months from the filing date. In some instances, the content of U.S. patent applications remains unavailable to the public until the patents are issued. As a result, we can never be certain that programs that we commence will be free of third party intellectual property rights. If we become aware of the existence of third party intellectual property rights only after we have commenced a particular program, we may have to forgo such project after having invested substantial resources in it.

We may infringe third party rights and may become involved in litigation, which may materially harm our business.

If a third party accuses us of infringing its intellectual property rights or if a third party commences litigation against us for the infringement of patent or other intellectual property rights, we may incur significant costs in defending such action, whether or not we ultimately prevail. Typically, patent litigation in the pharmaceutical and biotechnology industry is expensive and prolonged. Costs that we may incur in defending third party infringement actions would also result in the diversion of management's and technical personnel's time. In addition, parties making claims against us may be able to obtain injunctive or other equitable relief that could prevent us or our collaborators and licensees from further developing our discoveries or commercializing our products. In the event of a successful claim of infringement against us, we may be required to pay damages or obtain one or more licenses from the prevailing third party, which may not be available to us on commercially reasonable terms, if at all. If we are not able to obtain such a license or not able to obtain such a license at a reasonable cost, we could encounter delays in product introductions and loss of substantial resources while we attempt to develop alternative products. Defense of any lawsuit or failure to obtain any such license could prevent us or our partners from commercializing available products and could cause us to incur substantial expenditures.

Patent reform and other legislative changes in the U.S. and other countries may affect our ability to obtain and enforce our patents.

In 2011, the United States passed comprehensive patent reform laws in the "America Invents Act", or the "Act". These changes may affect our ability to obtain and enforce patents in a number of ways. First, the Act provides for a period of ex parte post-grant review with expanded grounds for challenging validity of a patent for nine months after grant of a patent. If the validity of one of our U.S. patents is successfully challenged, some or all of the claims may be invalidated, such that we could not enforce the patent and hence may not be able to protect one or more of our therapeutic product candidates. Other countries may also pass legislative changes to their patent laws which could materially affect – and even invalidate – one or more of our already filed patent applications, or even granted patents.

Increased progress in our scientific and technological environment may reduce our chances of obtaining a patent.

In order to obtain a patent to protect one of our therapeutic product candidates, we must show that the underlying invention (that is, the product candidate itself or its use) is inventive. As an increasing amount of scientific knowledge is becoming available regarding genes, proteins and biological mechanisms, the bar is increasingly raised to show sufficient inventiveness, as inventiveness is judged against all publicly available information available prior to filing of the patent application (the exact date may vary by country or due to other circumstances). We were initially pioneers in a largely unexplored field, but now there are many others working in our area. We may not be able to obtain patents for our product candidates due to the increased information published in this area. Collective patent applications, in which a large number of candidates are included in one patent application, are also challenged due to the raised bar for information that must be included in a patent application, as well as due to the availability of other publications. Our own published patent applications and other publications also serve as prior art against our new inventions and patent applications, and may prevent us from obtaining new patents.

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We may become subject to claims for remuneration or royalties for assigned service invention rights by our employees, which could result in litigation and adversely affect our business.

We enter into assignment of invention agreements with our employees pursuant to which such individuals agree to assign to us all rights to any inventions created in the scope of their employment or engagement with us. A significant portion of our intellectual property has been developed by our employees in the course of their employment for us. Under the Israeli Patent Law, 5727-1967, or the Patent Law, inventions conceived by an employee due to and during his or her employment with a company are regarded as "service inventions", which belong to the employer, absent a specific agreement between the employee and employer giving the employee service invention rights or waiver of such rights by employer. The Patent Law also provides that if there is no agreement with respect to whether the employee is entitled to remuneration for his or her service invention, to what extent and under what conditions, such entitlement and terms shall be determined by the Israeli Compensation and Royalties Committee, or the Committee, a body constituted under the Patent Law. Recent decisions by the Committee and Israeli courts have created some uncertainty in this area. Although our employees have agreed to assign to us service invention rights, we may face claims demanding remuneration in consideration for assigned inventions. As a consequence of such claims, we could be required to pay additional remuneration or royalties to our current and/or former employees, or be forced to litigate such claims, which could negatively affect our business.

Risks Related to Operations in Israel

Conditions in the Middle East and in Israel may adversely affect our operations.

Our headquarters and part of our research and development facilities are located in Israel. Accordingly, we are directly influenced by the political, economic and military conditions affecting Israel. Specifically, we could be adversely affected by:

- hostilities involving Israel;
- a full or partial mobilization of the reserve forces of the Israeli army;
- the interruption or curtailment of trade between Israel and its present trading partners; and
- a downturn in the economic or financial condition of Israel.

Israel has been subject to a number of armed conflicts that have taken place between it and its Arab neighbors. While Israel has entered into peace agreements with both Egypt and Jordan, Israel has not entered into peace arrangements with any other neighboring countries. Furthermore, violent uprisings in recent years in some Arab countries in the Middle East and North Africa, including in Egypt, Syria and Jordan which border Israel, and the significant increase of hostile activities of ISIS, the Islamic State of Iraq and the Levant, in Syria, adjacent to Israel's northern border, and in the Sinai Peninsula, adjacent to Israel's southern border, all maintain a level of uncertainty in the region. Recent events in Iran, including reports of its continuing nuclear development program, have further heightened the antipathy between Israel and Iran.

Over the past several years there has been a significant deterioration in Israel's relationship with the Palestinian Authority and a related increase in violence, including continued hostilities related to the Gaza Strip, which is controlled by the Hamas militant group. Efforts to resolve the problem have failed to result in a permanent solution. In 2014 Israel experienced another round of armed conflict with Hamas in the Gaza Strip, with missiles reaching the south and the center region of the country. All of the above raise a concern as to the stability in the region which may affect the political and security situation in Israel and therefore could adversely affect our business, financial condition and results of operations. Further deterioration of relations with the Palestinian Authority, Hamas or countries in the

Middle East could disrupt international trading activities in Israel and may materially and negatively affect our business conditions and could harm our results of operations.

In addition, a number of our employees who are Israeli citizens are subject to an obligation to perform reserve military service. In case of further regional instability such employees who may include one or more of our key employees may be absent for extended periods of time which may materially adversely affect our business. Certain countries, as well as certain companies and organizations, primarily in the Middle East, continue to participate in a boycott of Israeli firms and others doing business with Israel and Israeli companies. The boycott, restrictive laws, policies or practices directed towards Israel or Israeli businesses could, individually or in the aggregate, have a material adverse effect on our business in the future.

We can give no assurance that the political and security situation in Israel, as well as the economic situation, will not have a material impact on our business in the future.

Our results of operations may be adversely affected by the exchange rate fluctuations between the dollar and the New Israeli Shekel.

We hold most of our cash, cash equivalents and short-term and long-term bank deposits in U.S. dollars but incur a significant portion of our expenses, principally salaries and related personnel expenses and administrative expenses for our Israeli based operations, in NIS. As a result, we are exposed to exchange rate fluctuations between the U.S. dollar and the NIS, which may have a material adverse effect on our financial condition. The U.S. Dollar devaluated against the NIS by 7.0% in 2013, in 2014 the U.S. Dollar appreciated against the NIS by 12% and in 2015 the U.S. Dollar appreciated against the NIS by 0.30%, and, as a result, our NIS denominated expenses were affected by these fluctuations.. We entered into foreign currency derivative contracts to hedge a portion of our anticipated NIS payroll and certain operation expenses. For more information, see Note 2u of our 2015 consolidated financial statements.

We may not be entitled to certain tax benefits.

We may be entitled to benefit in the future from certain government programs and tax legislation, particularly as a result of the 'Approved Enterprise' status granted to some of our operations by the Investment Center in the Israeli Ministry of the Economy and the 'Benefiting Enterprise' status that resulted from our eligibility for tax benefits under the Israel Law for Encouragement of Capital Investments, 1959 (an "Approved Enterprise", a "Benefiting Enterprise" and the "Investment Law", respectively). The availability of these tax benefits, however, is subject to certain requirements under the Investment Law including, among other things, making specified investments in fixed assets and equipment. The tax benefits that we anticipate receiving under our current "Approved Enterprises" and "Benefiting Enterprises" programs may not be continued in the future at their current levels or at all. To date, we have not actually received any such tax benefits because we have not yet generated any taxable income.

It may be difficult to enforce a U.S. judgment against us, or our officers and directors or to assert U.S. securities law claims in Israel.

We are incorporated under the laws of the State of Israel. Service of process upon our directors and officers, almost all of whom reside outside the United States, may be difficult to obtain within the United States. Furthermore, because the majority of our assets and investments, and almost all of our directors and officers are located outside the United States, any judgment obtained in the United States against us or any of them may not be collectible within the United States. Additionally, it may be difficult to enforce civil liabilities under U.S. federal securities laws in original actions instituted in Israel.

Israeli courts may refuse to hear a claim based on an alleged violation of U.S. securities laws reasoning that Israel is not the most appropriate forum to bring such a claim. In addition, even if an Israeli court agrees to hear such a claim, it is not certain whether Israeli law or U.S. law will be applicable to the claim. If U.S. law is found to be applicable, the content of applicable U.S. law must be proven as a fact by expert witnesses, which can be a time consuming and costly process. Certain matters of procedure will also be governed by Israeli law. There is little binding case law in Israel that addresses the matters described above.

Provisions of Israeli law may delay, prevent or make undesirable an acquisition of all or a significant portion of our shares or assets.

Israeli corporate law regulates mergers and requires that a tender offer be effected when certain thresholds of percentage ownership of voting power in a company are exceeded (subject to certain conditions). Further, Israeli tax considerations may make potential transactions undesirable to us or to some of our shareholders whose country of

residence does not have a tax treaty with Israel granting tax relief to such shareholders from Israeli tax. With respect to mergers, Israeli tax law allows for tax deferral in certain circumstances but makes the deferral contingent on the fulfillment of numerous conditions, including a holding period of two years from the date of the transaction during which certain sales and dispositions of shares of the participating companies are restricted. Moreover, with respect to certain share swap transactions, the tax deferral is limited in time, and when such time expires, the tax becomes payable even if no actual disposition of the shares has occurred. See “Item 10.B. Memorandum and Articles of Association—Change of Control.”

Furthermore, in accordance with the Restrictive Trade Practices Law, 1988 and under the Israeli law for the Encouragement of Industrial Research and Development of 1984 and regulations promulgated thereunder, which we refer to as the R&D Law, to which we are subject due to our receipt of grants from the Office of the Chief Scientist, or the OCS, approvals regarding a change in control (such as a merger or similar transaction) may be required in certain circumstances. For more information regarding such required approvals please see "Item 5. Operating and Financial Review and Prospects Finance – C. Research and Development, Patents and Licenses – The Office of the Chief Scientist."

These provisions of Israeli law could have the effect of delaying or preventing a change in control and may make it more difficult for a third party to acquire us or our shareholders to elect different individuals to our board of directors, even if doing so would be beneficial to our shareholders, and may limit the price that investors may be willing to pay in the future for our ordinary shares.

We received grants from the OCS that may restrict the transfer of know-how that we develop.

We have received research and development grants from the OCS. Therefore, even following full repayment of any OCS grants, and unless agreed otherwise by the applicable authority of the OCS, we must nevertheless continue to comply with the requirements of the R&D Law. Accordingly, the transfer to third parties of know-how or technologies developed under the programs submitted to the OCS and as to which we received the grants, or manufacturing or rights to manufacture based on and/or incorporating such know-how to third parties, might require the prior consent of the OCS, and may require certain payments of increased royalties to the OCS. Although such restrictions do not apply to the export from Israel of the Company's products developed with such know-how, they may prevent us from engaging in transactions with our affiliates, customers or other third parties outside Israel, involving product or other asset transfers, which might otherwise be beneficial to us. For more information regarding such restrictions please see "Item 5. Operating and Financial Review and Prospects Finance – C. Research and Development, Patents and Licenses – The Office of the Chief Scientist."

Being a foreign private issuer exempts us from certain SEC and NASDAQ requirements.

We are a "foreign private issuer" within the meaning of rules promulgated by the SEC. As such, we are exempt from certain provisions applicable to U.S. public companies including:

- the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q and current reports on Form 8-K;
- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- the provisions of Regulation FD aimed at preventing issuers from making selective disclosures of material information; and
- the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and establishing insider liability for profits realized from any "short-swing" trading transaction (a purchase and sale, or sale and purchase, of the issuer's equity securities within less than six months).

In addition, under the rules and regulations of The NASDAQ Stock Market, a foreign private issuer may follow its home country practice in lieu of certain NASDAQ listing requirements. For example, under NASDAQ's rules a company traded on the NASDAQ market is required to select director nominees either by independent directors constituting a majority of the board of directors or by a nominations committee comprised solely of independent directors. Under Israeli law, there is no such requirement to have an independent nominating committee or to have the

independent directors of a company select (or recommend for selection) director nominees. Consistent with Israeli law, we have elected that our Board of Directors handle this process. We are also not required to adopt a formal board resolution or charter addressing the director nominations process and such related matters as may be required under the U.S. federal securities laws, as NASDAQ requires for a U.S. issuer. In addition, pursuant to Israeli law, we seek shareholder approval for all corporate actions requiring such approval under the requirements of the Israeli Companies Law, 5759-1999, as amended together with all regulations promulgated thereunder (the "Companies Law"), which are different from the requirements for seeking shareholder approval under NASDAQ Listing Rule 5635. For a description of certain transactions requiring shareholder approval under the Companies Law see "Item 10. Additional Information — B. Memorandum and Articles of Association — Conflict of Interest." Furthermore, consistent with Israeli law, generally a quorum for an adjourned general meeting of shareholders of the Company, is any two shareholders present in person, by proxy or by proxy card at such meeting. As such, the quorum requirements for an adjourned meeting are different from the NASDAQ requirement that an issuer listed on NASDAQ have a quorum requirement that in no case be less than 33 1/3% of the outstanding shares of the company's common voting stock. Because of these SEC and NASDAQ exemptions, investors are not afforded the same protections or information generally available to investors holding shares in public companies organized in the United States.

Your rights and responsibilities as a shareholder will be governed by Israeli law which differs in some material respects from the rights and responsibilities of shareholders of U.S. companies.

Because we are incorporated under Israeli law, the rights and responsibilities of our shareholders are governed by our Articles of Association ("Articles") and Israeli law. These rights and responsibilities differ in some respects from the rights and responsibilities of shareholders in U.S.-based corporations. In particular, a shareholder of an Israeli company has a duty to act in good faith and in a customary manner in exercising its rights and performing its obligations towards the company and other shareholders and to refrain from abusing its power in the company, including, among other things, in voting at the general meeting of shareholders on certain matters, such as an amendment to a company's articles of association, an increase of a company's authorized share capital, a merger of a company and approval of related party transactions that require shareholder approval. A shareholder also has a general duty to refrain from discriminating against other shareholders. In addition, a controlling shareholder or a shareholder who knows that it possesses the power to determine the outcome of a shareholders' vote or to appoint or prevent the appointment of an office holder in a company or has another power with respect to a company, has a duty to act in fairness towards such company. Israeli law does not define the substance of this duty of fairness and there is limited case law available to assist us in understanding the nature of this duty or the implications of these provisions. These provisions may be interpreted to impose additional obligations and liabilities on our shareholders that are not typically imposed on shareholders of U.S. corporations.

Risks Related to our Ordinary Shares

Holders of our ordinary shares who are U.S. residents may be required to pay additional U.S. income taxes if we are classified as a PFIC for U.S. federal income tax purposes.

There is a risk that we may be classified as a passive foreign investment company, or PFIC. Our treatment as a PFIC could result in a reduction in the after-tax return of U.S. holders of our ordinary shares and may cause a reduction in the value of our shares. For U.S. federal income tax purposes, we will generally be classified as a PFIC for any taxable year in which either: (i) 75% or more of our gross income is passive income or (ii) at least 50% of the average value (determined on a quarterly basis) of our total assets for the taxable year produce or are held for the production of passive income. Based on our analysis of our income, assets, activities and market capitalization, we do not believe that we were a PFIC for the taxable year ended December 31, 2015. However, there can be no assurances that the United States Internal Revenue Service ("IRS") will not challenge our analysis or our conclusion regarding our PFIC status. There is also a risk that we were a PFIC for one or more prior taxable years or that we will be a PFIC in future years, including 2016. If we were a PFIC during any prior years, U.S. holders who acquired or held our ordinary shares during such years generally will be subject to the PFIC rules. The tests for determining PFIC status are applied annually and it is difficult to make accurate predictions of our future income, assets, activities and market capitalization, which are relevant to this determination. If we were determined to be a PFIC for U.S. federal income tax purposes, highly complex rules would apply to U.S. holders owning our ordinary shares and such U.S. holders could suffer adverse U.S. tax consequences. For more information please see "Item 10. Additional Information – E. Taxation - Certain Material U.S. Federal Income Tax Considerations – Passive Foreign Investment Company."

Sales under our existing shelf registration statement will dilute existing shareholders.

On August 26, 2014, we filed a shelf registration statement on Form F-3 with the SEC under which we may offer and sell from time to time in one or more offerings, our ordinary shares, debt securities, rights, warrants and units comprising any combination of these securities having an aggregate offering price of up to $200 million ("the 2014 Shelf Registration"). This registration statement was declared effective by the SEC on September 4, 2014. As of February 1, 2016 no securities have been issued pursuant to the 2014 Shelf Registration. While there is no assurance that we will sell any shares, including shares underlying securities convertible into, exchangeable for, exercisable for shares, under this shelf registration statement, any such sales in the future may result in dilution to existing

shareholders. In addition, we may seek additional capital by selling shares or other securities under these shelf registration statements due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our ordinary shares are traded on more than one market and this may result in price variations.

In addition to being traded on The NASDAQ Global Market, our ordinary shares are also traded on the Tel Aviv Stock Exchange, or TASE. Trading in our ordinary shares on these markets take place in different currencies (U.S. dollars on NASDAQ and NIS on the TASE), and at different times (resulting from different time zones, trading days and public holidays in the United States and Israel). The trading prices of our ordinary shares on these two markets may differ due to these and other factors. Any decrease in the price of our ordinary shares on one market could cause a decrease in the trading price of our ordinary shares on the other market.

Our share price and trading volume have been volatile and may be volatile in the future and that could limit investors' ability to sell our shares at a profit and could limit our ability to successfully raise funds.

During the calendar years 2014 and 2015, our stock price on NASDAQ has traded from a low of $4.64 to a high of $14.32 and trading volume is volatile from time to time. The volatile price of our shares and periodic volatile trading volume may make it difficult for investors to predict the value of their investment, to sell shares at a profit at any given time, or to plan purchases and sales in advance. A variety of factors may affect the market price of our ordinary shares including:

- global macroeconomic developments;
- our success (or lack thereof) in entering into collaboration agreements and achieving certain research and developmental milestones thereunder;
- our need to raise additional capital and our success or failure in doing so;
- achievement or denial of regulatory approvals by us or our competitors;
- announcements of technological innovations or new commercial products by our competitors;
- developments concerning proprietary rights, including patents;
- developments concerning our existing or new collaborations;
- regulatory developments in the United States, Israel and other countries;
- delay or failure by us or our partners in initiating, completing or analyzing pre-clinical or clinical trials or the unsatisfactory design or results of such trials;
- period to period fluctuations in our results of operations;
- changes in financial estimates by securities analysts;
- changes in senior management or the board of directors;
- our ability (or lack thereof) to disclose the commercial terms of, or progress under, our collaborations;
- our ability (or lack thereof) to show and accurately predict revenues; and
- transactions with respect to our ordinary shares by insiders or institutional investors.

We are not able to control many of these factors, and we believe that period-to-period comparisons of our financial results will not necessarily be indicative of our future performance.

In addition, the stock market in general, and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that may be unrelated or disproportionate to the operating performance of individual companies. These broad market and industry factors may seriously harm the market price of our ordinary shares, regardless of our operating performance.

Furthermore, the market prices of equity securities of companies that have a significant presence in Israel may also be affected by the changing security situation in the Middle East and particularly in Israel. As a result, these companies may experience volatility in their stock prices and/or difficulties in raising additional financing required to effectively operate and grow their businesses. Thus, market and industry-wide fluctuations and political, economic and military conditions in the Middle East may adversely affect the trading price of our ordinary shares, regardless of our actual operating performance.

As a result of the volatility of our stock price, we could be subject to securities litigation, which could result in substantial costs and divert management's attention and company resources from our business.

ITEM 4.INFORMATION ON THE COMPANY

A. HISTORY AND DEVELOPMENT OF THE COMPANY

History

Our legal and commercial name is Compugen Ltd. We were incorporated on February 10, 1993 as an Israeli corporation and operate under the Israeli Companies Law. Our principal offices are located at 26 Harokmim Street, Holon 5885800, Israel, and our telephone number is +972-3-765-8585. Our web address is www.cgen.com. Information contained on our website does not constitute a part of this annual report.

Our agent for service of process in the United States is Compugen USA, Inc., our wholly owned U.S. subsidiary located at 250 E. Grand Avenue, Suite 65, South San Francisco, CA 94080, which was incorporated in Delaware in March 1997 and is qualified to do business in California. This subsidiary did not have any significant operations from 2008 to March 2012.

Principal Capital Expenditures

In the years ended December 31, 2015, 2014 and 2013, our capital expenditures were $4.4 million, $2.2 million and $328,000, respectively, and for the year 2015 were spent primarily on leasehold improvements for the new facilities in Holon, Israel (see Item 4D - Property, Plants and Equipment), laboratory equipment, general computer software and hardware. As of December 31, 2015, other than $1.3 million which are included within the $4.4 million capital expenditures for the year ended December 31, 2015 but not yet paid as of that date, we have no current significant commitments for capital expenditures.

B. BUSINESS OVERVIEW

Overview

Compugen is a leading therapeutic discovery company utilizing its broadly applicable predictive discovery infrastructure to identify novel drug targets and develop first-in-class biologics. The Company's current pipeline primarily consists of early-stage immuno-oncology programs aimed at harnessing the immune system to fight cancer.Our pipeline's focus is on immune checkpoint target candidates discovered by us, which are predicted to serve as promising drug targets for cancer immunotherapies addressing various cancer types and patient populations, both as monotherapy and in combination with other drugs. Our business model relies on extracting the commercial value of our systematic discovery capability by entering into various forms of revenue-sharing collaborations for our novel drug target candidates and therapeutic product candidates at various stages of research and development. Compugen is headquartered in Holon, Israel, with R&D facilities located in both Holon and South San Francisco. At the U.S. facilities, therapeutic monoclonal antibodies (mAbs) are discovered and developed against our novel drug target candidates.

Predictive Discovery of Novel Targets

The establishment of our broadly applicable discovery approach evolved over a decade of pioneering multidisciplinary research involving in-depth understanding of key biological phenomena combined with the development of superior computational modeling capabilities. This approach, which is constantly enhanced and broadened, has been designed to allow us to focus on a selected biomedical field of research, and to emerge with a set

of novel drug targets that otherwise would have been challenging to identify. We employ our discovery approach in multiple therapeutic and diagnostic areas and have demonstrated significant advantages of our methodologies in terms of ability to discover novel target candidates, cost, time and probability of successful experimental validation, in comparison to traditional discovery methods.

Therapeutic/Disease Fields of Focus

Oncology and immunology (autoimmune diseases) are two medical fields with significant unmet medical needs. Biologics, such as mAb and Fc-fusion proteins, have revolutionized patients' treatment in these two disease areas and have demonstrated substantial clinical benefit and commercial success. Compugen has chosen these two growing disease areas as its focus for its broadly applicable predictive capabilities. Biologics are one of the fastest growing segments in the drug industry and made up 27% of 2014 FDA approvals. Seven of the top ten selling drugs in 2014 were biologics including Humira (adalimumab), the top selling drug in 2014 with sales of $12.5 billion, Remicade (infliximab) and Rituxan/MabThera (rituximab), all indicated for the treatment of arthritis. Additionally, biologics to treat cancer represented three of the top ten best-selling drugs in 2014, and included Rituxan, Herceptin and Avastin.

For these reasons oncology and autoimmune diseases continue to be disease areas of high interest to pharmaceutical companies with numerous efforts to identify novel therapeutic solutions. Our science-driven predictive capabilities are well suited for the identification of novel target candidates suitable for therapeutic intervention for these complex, multi-factorial diseases. In recent years, we further focused our activities to be mainly in the field of immuno-oncology, an area of high medical promise and industry interest, where the modulation of the immune system has shown notable clinical success in treating various types of cancer.

Monoclonal Antibody Therapy for Oncology

mAb therapeutics is a class of biological drugs that harnesses the exquisite specificity and potent binding properties of antibodies to create a mono-specific antibody (drug) that binds to the drug target of interest with high specificity and thereby limits the potential for off-target toxicity that is often seen with small molecule drugs. The extremely large repertoire of possible mAb that can be generated means that one can generate highly specific mAb drug candidates that can: a) bind to almost any extracellular or cell surface target protein; b) bind and antagonize the target of interest or c) bind and agonize the target of interest. Due to the versatility and high specificity of this approach, mAb therapies are being intensively researched, developed and commercialized as treatments for numerous serious diseases with the belief that they have the potential to be more effective treatments with fewer side effects compared to traditional small molecule chemical drugs. During the past two decades, mAbs have emerged as an important and rapidly growing drug class, with over 20 mAbs already approved for therapeutic use in the United States for various clinical indications, including oncology, chronic inflammatory diseases, transplantation, infectious diseases and cardiovascular diseases. For cancer therapy, a mAb may inhibit cellular processes critical for tumor growth, stimulate the patient's immune system to attack the target cancerous cells, or be used for targeted delivery of chemotherapy specifically to the cells identified by the antibodies (known ADC technology). Moreover, according to an analysis by Tufts University, the rate of success for mAb therapeutics from first use in humans to regulatory approval is more than double that of traditional small molecule chemical drugs.

Although significant progress has been made in recent years in mAb therapeutics, numerous challenges still remain. One of the main challenges in this extremely promising field of mAb therapeutics is the identification of novel extracellular or cell surface targets that can translate into clinically relevant therapies for a variety of disease indications. To this end, we have developed several proprietary target discovery platforms through focusing on and integration of various aspects of our unique predictive discovery capabilities to identify novel drug targets for mAb therapies. Our Pipeline Program activities are currently focused on mAbs as the therapeutic modality for cancer immunotherapy, with an additional Fc fusion therapeutics program for autoimmune diseases.

Therapeutic Proteins for Immunology

Therapeutic proteins are another type of biological drug, typically a large biological molecule or a fragment derived from a relevant extracellular or cell surface protein and usually engineered and produced by recombinant technologies to have drug-like properties. For example a cell surface or extracellular protein could be engineered to be fused to the Fc domain of an IgG (antibody) protein to provide a longer half-life in the blood. Therapeutic proteins are clinically used to treat a wide range of diseases including cancer, autoimmune diseases, infectious diseases, blood-related disorders and others. CGEN-15001, our lead program for autoimmune diseases, is an Fc fusion protein. This class of therapeutic proteins, known as Fc fusion proteins, has achieved significant clinical and commercial success as exemplified by the anti-rheumatic biologics ENBREL® (etanercept) with sales of about $8.9 billion in 2014, and ORENCIA® (abatacept) with about $1.6 billion in sales in 2014.

The Pipeline Program

In order to leverage our capability to predict multiple novel drug targets with each discovery effort, we established our Pipeline Program to allow the parallel target validation and early development of multiple therapeutic candidates based on such targets. Our Pipeline Program currently ranges from target validation to pre-clinical studies in the fields of oncology and immunology, with a primary focus on immuno-oncology. The aim of the Pipeline Program is to advance the validation of Compugen-discovered drug target candidates to generate therapeutic drug candidates against such targets – mainly as mAb therapeutics or to a lesser extent as Fc fusion protein therapeutics - and to further advance selected therapeutic candidates beyond their animal proof of concept stage. The newly discovered target candidates enter the Pipeline Program when they begin experimental evaluation following their in silico prediction and selection and undergo various experimental validation studies to confirm their therapeutic potential. The experimental

validation studies are conducted at our facilities, or at external expert laboratories, selected specifically for each relevant field. This is followed by the generation of a therapeutic product candidate to be used for in vitro and in vivo proof of concept studies in disease animal models, as applicable. Therapeutic Fc fusion proteins or mAb product candidates, either humanized or fully-human, then enter the stage of lead candidate selection and optimization, with a final lead to be advanced to investigational new drug application (IND) enabling studies. For selected therapeutic product candidates we intend to continue development into early clinical development. Our strategy is to partner our novel drug target candidates and their respective therapeutic product candidates in our Pipeline Program will be partnered at different stages of the drug development process, under collaborative and/or licensing arrangements of different types with third parties.

Pipeline Program

Overview

During 2010, we integrated our approach to novel target discovery, moving from a "technology driven" individual platform based methodology to a "therapeutics needs (market) driven" approach. In this "therapeutics needs (market) driven" approach, we harnessed all of our relevant discovery platforms, systems and tools towards a selected unmet need in order to predict and validate novel target candidates that we believed have the highest potential to generate successful first-in-class drug candidates to address that particular need. With our primary focus in immuno-oncology, we believe this approach will enable us to make significant contributions to oncology treatment. In late 2010, we initiated our Pipeline Program, pursuant to which we both (i) accelerated the number of predicted and selected drug target candidates being evaluated by us, primarily in our fields of focus, and (ii) took certain therapeutic product candidates further beyond their proof of concept into preclinical activities In selected cases, assuming continued preclinical success, we intend to take them into early clinical development.

First Focused Discovery Program – Immune Checkpoints

Modulation of the immune system has shown clinical success in several therapeutic applications, such as treating various types of cancer, inhibiting autoimmune diseases and prolonging graft survival in organ transplant recipients. This increasing clinical significance is the basis for significant interest in the discovery and development of immunomodulators for therapeutic uses, and the rationale behind Compugen's first therapeutic needs driven efforts: the identification of novel immune checkpoint protein candidates that can serve as targets for therapeutic mAb discovery or be engineered to produce therapeutic product candidates.

Our first focused discovery program was directed towards the discovery of novel members of the immune checkpoint regulators family of proteins, initially specifically focusing on B7/CD28 co-stimulatory/co-inhibitory proteins, which are of high interest to the industry and have therapeutic potential in both cancer and autoimmune diseases. As a result of this successful discovery effort, the primary focus of our Pipeline Program is mAb therapeutics targeting these potential B7/CD28 like checkpoint candidates for cancer immunotherapy, and to a lesser degree, Fc fusion protein therapeutics for autoimmune diseases based on these novel checkpoint candidates.

Our initial results in identifying potential B7/CD28-like immune checkpoint candidates and the high industry interest in this class of proteins, led us to expand our discovery efforts to the identification of additional sets of immunomodulatory proteins beyond this family. By extending our predictive discovery capabilities for immunotherapy, we developed a methodology designed to discover immunomodulators distinct from B7/CD28-like proteins. During 2014, we demonstrated successful initial experimental results for one of these novel immunomodulatory target candidates that had been predicted in silico. Some of the other target candidates are in validation stage. In addition, during 2013 we successfully undertook our second focused discovery effort in the area of targets for antibodydrug conjugate or ADC technology, and in 2015 announced potent in-vitro cyotoxic activity by an exemplary ADC antibody developed by us against CGEN-15027 as an ADC target, with additional programs either at the therapeutic antibody discovery and development or the validation stage.

Immune checkpoints:

Immune checkpoints are negative regulators of the immune system, that play critical roles in maintaining self-tolerance, preventing autoimmunity and protecting tissues from immune collateral damage. These immune checkpoints are often "hijacked" by tumors to restrain the ability of the immune system to mount an effective anti-tumor response. Blocking immune checkpoints provides a promising approach for activating anti-tumor immunity. Indeed, recent FDA approval of antibody-based drugs blocking the immune checkpoints CTLA4 and PD-1 has emerged as a paradigm shift in cancer therapy, leading to durable clinical responses even in patients with advanced cancer. The

breakthrough successes in melanoma, lung and kidney cancers provided therapeutic validation for this approach and formed the foundation for a new era of cancer immunotherapy. Despite the success of CTLA4 and PD-1 blockers, many patients do not respond to these treatments and the clinical benefit is still limited to a small subset of cancer indications. In those indications where a response is seen it is typically only a minority of patients that achieve the promise of long-term survival. It is therefore clear there are additional immune evasion mechanisms mediated by other immune checkpoint proteins. The activity of the immune system is mostly regulated by immune cells called T cells. One protein family which is responsible for regulating immune cells, including T cells, is the B7/CD28 family of co-stimulatory and co-inhibitory receptors and ligands. Naïve T cells are initially activated by antigens derived from invading pathogens or from malfunctioning cells, such as cancer cells. The magnitude and efficacy of the immune response is determined by a delicate balance between co-stimulatory and co-inhibitory signals. Tumors exploit this regulatory mechanism by continuously inducing co-inhibitory signals (immune checkpoints) to evade immune destruction. Therefore, the ultimate goal of cancer immunotherapy is to enable the immune system to detect cancerous cells, destroy them and prevent further tumor development.

There are currently three therapies approved for the treatment of cancer that target immune checkpoint proteins. Yervoy®, an antibody treatment targeting CTLA-4, was approved by the FDA in 2011 and registered 2014 sales of $1.3 billion dollars, representing an increase of approximately 35% over 2013 sales. In September 2014, Keytruda®, an antibody therapy targeting PD-1, received accelerated approval from the FDA for the treatment of advanced melanoma and was approved for non-small cell lung cancer (NSCLC) in October 2015. Opdivo®, an antibody therapy targeting PD-1 was first approved for the treatment of advanced melanoma in December 2014 and was approved for non-small cell lung cancer (NSCLC) in October 2015 and renal cell carcinoma in November 2015. These therapies, along with many additional immune checkpoint targeting programs, are currently in advanced clinical trials in a large number of cancer indications with significant unmet need. Industry analysts estimate that the cancer immunotherapy market has a significant potential and annual sales' projections of some of these analysts range between $28 billion and $35 billion.

Predictive discovery of novel immune checkpoints for immuno-oncology:

A key Compugen established capability in this field was the development and use of our Predictive Discovery Platforms for the discovery of novel protein members belonging to various known and clinically important protein families. These discovery platforms incorporate two key Compugen proprietary infrastructure capabilities: LEADS and MED (described in more detail below). Specialized algorithms designed for identification of the unique characteristics of specific protein families, utilizing LEADS and MED, analyze the entire proteome to search for novel proteins belonging to a desired family. This platform concept was initially developed for the identification of novel immunomodulators which can serve as protein therapeutics for various pathological conditions, and more specifically, the B7/CD28 protein family of costimulators/coinhibitors. The reason we focused initially on this protein family is that B7/CD28 proteins are known to play key roles in regulating immune responses and serve as immune checkpoints. Also, there is a very low homology between these family members, which we believed we could overcome by using our unique approach. We believe new proteins belonging to this family could have significant therapeutic potential in many pathological conditions, including oncology, infectious disease, and autoimmune diseases. Applying the Predictive Discovery Platforms resulted in the identification of a number of putative immune checkpoint B7/CD28-like protein candidates, of which those that we have disclosed are CGEN-15001T, CGEN-15022, CGEN-15029, CGEN-15049, CGEN-15027 CGEN-15052 and CGEN-15092.

In order to discover the immunomodulators distinct from B7/CD28-like proteins, we used a new discovery capability that incorporates the predictive modeling of two distinct biological phenomena related to the role of the immune system that are conceptually different from those employed in the discovery of Compugen's B7/CD28-like candidates. The first biological phenomenon that was modeled exploits the interplay between the immune system and intruding pathogens. As a result of such interplay, some immune proteins tend to evolve differently from non-immune related ones. We devised an evolutionary model to detect such potential immune proteins, and this predictive algorithm was incorporated into our discovery infrastructure and integrated with our existing tools for the discovery of target candidates for cancer immunotherapy. The second biological phenomenon was modeled on the biology of tumor-associated macrophages (TAMs). TAMs are an important component of the tumor microenvironment and play a major role in creating the immunosuppressive environment that enables tumor development. Proteins having the potential to modulate the tumor microenvironment may serve as potential targets for cancer immunotherapy. The modeling of this second biological phenomenon relies heavily on our MED Platform, which was employed to predict proteins that may play a role in the TAMs biology.

Target characterization and validation and therapeutic discovery and development of our immune checkpoint candidates:

During 2014 and 2015 we enhanced our target characterization and validation infrastructure, as well as our therapeutic discovery and development efforts, in order to be able to advance multiple immune checkpoint candidates in our Pipeline Program. We added personnel, equipment, new experimental systems and technologies to increase expertise

and workload throughput. Furthermore, in addition to our internal expansion efforts, we entered into new or expanded agreements with leading contract research organizations and academic research centers.

In December 2014, we signed a multi-year research collaboration with Johns Hopkins University, School of Medicine, under the direction of Prof. Drew Pardoll and Dr. Charles Drake. Prof. Pardoll and Dr. Drake, members of Compugen's Scientific Advisory Board, are pioneers in the field of immuno-oncology. The collaboration focuses on further evaluation of selected novel B7/CD28-like immune checkpoint candidates discovered by us for the potential treatment of cancer. This evaluation includes the candidates' differentiation profile with respect to known checkpoints and their potential to serve either for monotherapy or in combination with other cancer treatments. This collaborative research will expand our ongoing assessment of the biology and mechanism of actions of our novel B7/CD28-like immune checkpoint candidates, and provide access to the world-class immuno-oncology research tools and expertise at Johns Hopkins University. In January 2015, we signed an agreement with the U.S. National Institutes of Health (NIH) according to which we obtained rights to use certain biological systems and materials developed by the NIH in-house for purposes of advancing the research and development of our multiple immuno-oncology programs toward future clinical evaluation. The experimental systems and biological materials obtained from the NIH enable the engineering of human T cells to specifically recognize tumor antigens on cancer cells. Together with the collaboration with Johns Hopkins University, these new capabilities provide us with various capabilities and technologies to advance in parallel multiple immune checkpoint target programs toward the development of first-in-class biologics.

First Focused Discovery Program output: Immune checkpoint target candidates:

Our first validated drug target candidate, CGEN-15001T, was found to be expressed in several cancers, such as Hodgkin's lymphoma and Non-Hodgkin's lymphoma. A second drug target candidate, CGEN-15022, was found to be expressed in numerous types of epithelial cancers with significant unmet clinical needs, such as liver, colorectal, lung and ovarian cancers. The different expression profiles of CGEN-15022 and CGEN-15001T not only provide important differentiating characteristics between these two novel drug target candidates, but also offer promising potential to utilize these proteins as mAb targets to treat a broad set of key cancer indications with significant unmet medical needs. In August 2013, we signed a research and discovery collaboration and license agreement with Bayer for the development and commercialization of antibody-based therapeutics for cancer immunotherapy against CGEN-15001T and CGEN-15022.

In June 2015, we disclosed experimental validation data for CGEN-15029, a novel B7/CD28-like immune checkpoint target candidate. Initial validation studies show that expression of CGEN-15029 in T-cells inhibits their activation by melanoma cells, consistent with an immune suppressive role of the target in the tumor microenvironment. The target possesses signature immune-checkpoint receptor characteristics, including expression in relevant subsets of T- and NK-cells, with particularly high expression in lymphocytes that populate the tumor microenvironment (known as tumor infiltrating lymphocytes or TILs). A binding partner for CGEN-15029 has also been identified, which enables a clear path towards selection of inhibitory antibodies and their therapeutic development. CGEN-15029 is our highest priority mAb program and was selected to be advanced toward clinical testing.

In September 2013, we first disclosed experimental data for CGEN-15049, a novel immune checkpoint target candidate. CGEN-15049 was shown to inhibit the activity of immune cells that play important roles in immune responses against cancer, such as natural killer cells (NKs) and tumor antigen-specific cytotoxic T lymphocytes (CTLs), including TILs from melanoma patients. Furthermore, CGEN-15049 was shown to promote differentiation of inducible regulatory T cells (iTregs), a major cellular component of the immunosuppressive tumor microenvironment. In November 2015 we announced that a decision was made with respect to CGEN-15049 to perform additional target validation research to re-assess the target's mode of action.

First disclosed in 2014, in September 2015, we disclosed new target validation results for CGEN-15052, a novel immune checkpoint target candidate. CGEN-15052 has demonstrated in several experimental settings robust inhibition of T cell activation, both as a membrane protein and as an Fc fusion protein. Furthermore, recombinant expression of CGEN-15052 on cancer cells in a syngeneic mouse animal model enhances tumor growth compared with control cancer cells not expressing CGEN-15052.

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In October 2014, we disclosed successful experimental data for CGEN-15027, a novel immune checkpoint target candidate. CGEN-15027 was initially disclosed as one of the multiple immune checkpoint target candidates discovered in the Company's first focused predictive discovery program. In a subsequent discovery program, the protein was also predicted to be a potential ADC target. Experimental evaluation of CGEN -15027, including the prediction and validation of high expression levels of CGEN-15027 in lung, breast, ovarian, and pancreatic tumors as compared to normal tissues, strengthened its potential as a target for ADC therapy. In addition, the ability of an exemplary ADC to mediate potent killing of cancer cell lines expressing this protein was demonstrated using therapeutic antibodies for CGEN-15027. The expression and functional data provide further validation of the target, and suggest broad first-in-class clinical potential of CGEN-15027 antibodies in treating multiple solid tumor types. Based on these results, our research development focus on this novel candidate has moved to ADCs as a therapeutic product candidate.

Some of our immune checkpoint mAb target candidates were engineered as recombinant proteins consisting of the extracellular region of the immune checkpoint membrane proteins' candidate fused to an Fc antibody domain. CGEN-15001 was the first of these predicted candidates to undergo extensive in vitro and in vivo validation. In 2015, we continued to expand our activities in the field of immuno-oncology and continued to commit a higher portion of our resources to immuno-oncology rather than immunology. In the field of immunology we focused on CGEN-15001 in further elucidating its unique mechanism of action and in studying its translational potential using biological samples from autoimmune patients. See below: "Fc Fusion therapeutics: Immune checkpoint candidates."

Second Focused Discovery Program – Targets for Antibody Drug Conjugate Technology

Antibody-drug conjugate (ADC) cancer therapy destroys cancer cells by harnessing the highly specific binding of a mAb to deliver high-potency cytotoxic agents, called the payload, directly to the cancer cells. The principle underlying ADC therapy is to use the selective binding of a mAb to impact only the cancer cells by linking the cytotoxic agent payload to an antibody or antibody fragment that specifically binds to a protein that is present on cancer cells and expressed at lower levels in healthy cells. When administered to the patient, the antibody with the payload specifically binds to the protein of interest (the target), and upon binding the mAb and its payload are internalized into the cells, where the toxic payload is released and activated. Thus, unlike traditional chemotherapies, ADCs are designed to specifically destroy only cells displaying the cancer target protein. ADCs against a number of targets, both in solid and hematologic tumors, have already demonstrated clinical success, with two ADC products gaining FDA approval since 2011.

Fueled by the success of recent FDA approvals, ADC cancer therapy is an area of increased focus and activity and there are approximately 50 ADCs currently in clinical testing. ADC therapeutics generated approximately $1 billion of sales in 2014 and the ADC market is forecast to grow to $10.4 billion dollars by 2024 (Roots Analysis 2014).

Arming antibodies or antibody fragments with cytotoxic agents can be viewed as a means of enhancing tumor cell killing while sparing normal cells. ADCs represent a potential approach to enhance the efficacy of mAbs, by harnessing the mAb specificity to target the delivery of a cytotoxic agent to the tumor. Cancer therapy through ADCs addresses an area of high unmet medical need and is of great interest to the pharma industry. Only a limited number suitable ADC targets have been identified to date, and there is need for more ADC targets with superior characteristics, which provides an opportunity for Compugen to serve as a key source for the next generation of such potential targets.

Compugen's ADC target discovery program, which was initiated in 2013, utilizes our underlying predictive discovery infrastructure, with the addition of certain algorithms and other computational capabilities specifically developed for this effort. The additional algorithms enable prediction of cell surface/membrane proteins that have the potential to be internalized, and have higher expression on cancer cells but have much lower expression on healthy cells, in order to allow the ADC drug to selectively attack the tumor and spare healthy tissues. Additional parameters were included to

enhance to identification of targets associated with advanced cancer stages and poor clinical outcome, in order to provide potential superior first-in-class treatment to patient populations with limited therapeutic options and high unmet need.

Second Focused Discovery Program output: ADC target candidates:

The initial results from our second focused in silico discovery program, potential candidate targets for ADC cancer therapy, were announced at the end of 2013. In January 2015, we announced that two of the in silico predicted targets for ADC cancer therapy demonstrate low expression levels in normal critical tissues, such as heart and liver, and higher expression in multiple cancer types, such as colorectal and prostate cancers, for which there is high unmet medical need. These results suggest that these two drug target candidates have potential to serve for the development of ADC therapy in oncology. In October 2015 we announced that CGEN-15027, initially disclosed as an immune checkpoint target candidate, was also predicted to be a potential ADC target in a subsequent discovery program. Further evaluation of CGEN -15027 as a target for ADC therapy, including the prediction and validation of is high expression levels of CGEN-15027 in lung, breast, ovarian, and pancreatic tumors as compared to normal tissues, strengthened its potential as an ADC target. Using therapeutic antibodies for CGEN-15027 developed by us, we demonstrated the ability of an ADC to mediate potent killing of cancer cell lines expressing this protein.

The Pipeline Program: Novel Drug Target Candidates and Therapeutic Product Candidates