Galmed Pharmaceuticals Ltd.
Form 20-F
March 22, 2016

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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Form 20-F

..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

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

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

Commission File No. 001-36345

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GALMED PHARMACEUTICALS Ltd.

(Exact name of Registrant as specified in its charter)

N/A

(Translation of the Registrant's name into English)

State of Israel

(Jurisdiction of incorporation)

16 Ze'ev Tiomkin Street, Tel Aviv, Israel 6578317

(Address of principal executive offices)

Allen Baharaff

President and Chief Executive Officer

16 Ze'ev Tiomkin Street

Tel Aviv, Israel 6578317

Tel: +972.3.693.8448

Fax: +972.3.693.8447

(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	**Nasdaq Capital Market**

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. I1,100,453

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

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. Yes ¨ No x

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 a shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x **No** ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, 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). Yes x **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 ¨ **Accelerated filer** ¨ **Non-accelerated filer** x

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). Yes ¨ **No** x

(APPLICABLE ONLY TO ISSUERS INVOLVED IN BANKRUPTCY PROCEEDINGS DURING THE PAST FIVE YEARS)

Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court. Yes ¨ **No** ¨

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ABOUT THIS ANNUAL REPORT

All references to "we," "us," "our," "the Company" and "our Company", in this Annual Report on Form 20-F, or our annual report, are to Galmed Pharmaceuticals Ltd. and its subsidiaries, unless the context otherwise requires. All references to "shares" or "ordinary shares" are to our ordinary shares, NIS 0.01 nominal par value per share. All references to "Israel" are to the State of Israel. "U.S. GAAP" means the generally accepted accounting principles of the United States. Unless otherwise stated, all of our financial information presented in this annual report has been prepared in accordance with U.S. GAAP. Any discrepancies in any table between totals and sums of the amounts listed are due to rounding. Unless otherwise indicated, or the context otherwise requires, references in this annual report to financial and operational data for a particular year refer to the fiscal year of our company ended December 31 of that year.

Our reporting currency and financial currency is the U.S. dollar. In this annual report, "NIS" means New Israeli Shekel, and "$," "US$" and "U.S. dollars" mean United States dollars.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 20-F contains forward-looking statements about our expectations, beliefs or intentions regarding, among other things, our product development efforts, business, financial condition, results of operations, strategies or prospects. In addition, from time to time, we or our representatives have made or may make forward-looking statements, orally or in writing. Forward-looking statements can be identified by the use of forward-looking words such as "believe," "expect," "intend," "plan," "may," "should," "anticipate," "could," "might," "seek," "project," "forecast," "continue" or their negatives or variations of these words or other comparable words or by the fact that these statements do not relate strictly to historical matters. These forward-looking statements may be included in, among other things, various filings made by us with the U.S. Securities and Exchange Commission, or the SEC, press releases or oral statements made by or with the approval of one of our authorized executive officers. Forward-looking statements relate to anticipated or expected events, activities, trends or results as of the date they are made. Because forward-looking statements relate to matters that have not yet occurred, these statements are inherently subject to risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements, including, but not limited to, the factors summarized below:

- the timing and cost of our ongoing Phase IIB ARREST Study and planned Phase III trials, for our product candidate, Aramchol™ (hereinafter referred to as "Aramchol") for the treatment of patients with overweight or obesity and who are pre diabetic or type II diabetic (hereinafter OD patients) with Non-Alcoholic Steato-Hepatitis, or NASH, or whether such trials will be conducted at all;

- completion and receiving favorable results of these Phase IIB and Phase III trials for Aramchol;

- regulatory action with respect to Aramchol by the U.S. Food and Drug Administration, or FDA, or the European Medicines Authority, or EMA, including but not limited to acceptance of an application for marketing authorization, review and approval of such application, and, if approved, the scope of the approved indication and labeling;

- the commercial launch and future sales of Aramchol or any other future products or product candidates;

- our ability to comply with all applicable post-market regulatory requirements for Aramchol in the countries in which we seek to market the product;

- our ability to achieve favorable pricing for Aramchol;

- our expectations regarding the commercial market for NASH in OD patients;

- third-party payor reimbursement for Aramchol;
- our estimates regarding anticipated capital requirements and our needs for additional financing;
- market adoption of Aramchol by physicians and patients;
- the timing, cost or other aspects of the commercial launch of Aramchol;
- the development and approval of the use of Aramchol for additional indications or in combination therapy; and
- our expectations regarding licensing, acquisitions and strategic operations.

We believe these forward-looking statements are reasonable; however, these statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. We discuss many of these risks in this annual report in greater detail under the heading "Risk Factors" and elsewhere in this annual report. Given these uncertainties, you should not rely upon forward-looking statements as predictions of future events.

All forward-looking statements attributable to us or persons acting on our behalf speak only as of the date hereof and are expressly qualified in their entirety by the cautionary statements included in this annual report. We undertake no obligations to update or revise forward-looking statements to reflect events or circumstances that arise after the date made or to reflect the occurrence of unanticipated events. In evaluating forward-looking statements, you should consider these risks and uncertainties.

EXPLANATORY NOTE

Market data and certain industry data and forecasts used throughout this Annual Report on Form 20-F were obtained from internal company surveys, market research, consultant surveys commissioned by the Company, publicly available information, reports of governmental agencies and industry publications and surveys. Industry surveys, publications, consultant surveys commissioned by the Company and forecasts generally state that the information contained therein has been obtained from sources believed to be reliable. However, this information may prove to be inaccurate because of the method by which some of the data for the estimates is obtained or because this information cannot always be verified with complete certainty due to the limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties. As a result, the market and industry data and forecasts included or incorporated by reference in this Annual Report on Form 20-F, and estimates

and beliefs based on that data, may not be reliable. We have relied on certain data from third-party sources, including internal surveys, industry forecasts and market research, which we believe to be reliable based on our management's knowledge of the industry. However, we have not ascertained the underlying economic assumptions relied upon therein. Forecasts are particularly likely to be inaccurate, especially over long periods of time. In addition, we do not necessarily know what assumptions regarding general economic growth were used in preparing the forecasts we cite. Statements as to our market position are based to the best of our knowledge on the most currently available data. While we are not aware of any misstatements regarding the industry data presented in this Annual Report on Form 20-F, our estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading "Risk Factors" in this annual report.

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 Financial Data.

The following table sets forth our selected consolidated financial data for the periods ended and as of the dates indicated, which reflects the financial data of Galmed Holdings Inc., a holdings company incorporated in the British Virgin Islands, or GHI, our predecessor, prior to the Reorganization (as defined below), as well as the financial data of the Company post Reorganization. The following selected consolidated financial data for our company should be read in conjunction with the financial information, "Item 5. Operating and Financial Review and Prospects" and other information provided elsewhere in this Annual Report on Form 20-F and our consolidated financial statements and related notes. The selected consolidated financial data in this section is not intended to replace the consolidated financial statements and is qualified in its entirety thereby. In the opinion of our management, our unaudited consolidated financial statements contain all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of our financial position, results of operations and cash flows as of and for the periods indicated therein.

We derived the selected consolidated financial statements as of and for the years ended December 31, 2015, 2014, 2013, 2012 and 2011, as applicable, from our audited consolidated financial statements included elsewhere in this Annual Report on Form 20-F.

	Year ended December 31,				
	2011	2012	2013	2014	2015
	(in thousands)				
Research and development expenses	$1,326	$2,443	$7,207	$6,664	$7,629
General and administrative expenses	151	694	7,355	2,478	3,246
Capital Loss	—	—	10	—	—
Operating loss	1,477	3,137	14,572	9,142	10,875
Financial expenses	3	6	2,912	10	180
Financial Income	—	—	—	(50)	(433)
Taxes on income	2	6	1	1	—
Net loss	$1,482	$3,149	$17,485	$9,103	$10,622
Comprehensive loss	1,482	3,149	17,485	9,099	10,832
Net loss per ordinary share	(*)**$0.30**	(*)**$0.63**	(*)**$3.45**	(*)**$0.88**	$0.96
Number of ordinary shares used in computing loss per ordinary share	(*)4,995,837	(*)4,995,837	(*)5,096,466	(*)10,323,686	11,101,453

(*) Retroactively adjusted to reflect the 729:1 share split, which occurred upon the consummation of the Reorganization (as defined below).

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Consolidated Balance Sheet data:	As of December 31, 2012	2013	2014	2015
	(In thousands)			
Cash and cash equivalents	$718	$137	$23,736	$4,156
Short-term deposits and marketable securities	—	—	8,250	18,845
Other receivables	14	16	165	379
Fixed assets	30	13	774	883
Total assets	762	166	32,925	24,263
Total liabilities	2,741	2,117	1,518	2,718
Total shareholders' equity	(1,979)	(1,951)	31,407	21,545
Number of ordinary shares issued and outstanding	4,995,837(*)	7,099,731(*)	11,100,453	11,100,453

(*) Retroactively adjusted to reflect the 729:1 share split, which occurred upon the consummation of the Reorganization (as defined below).

Exchange Rate

Galmed reports its financial results and balance sheet position in U.S. dollars. On March 10, 2016, the latest practicable date for inclusion in this report, the exchange rate between New Israeli Sheckels and U.S. dollars as published by the Bank of Israel was 3.90 NIS.

The average exchange rates for each of the five most recent fiscal years, calculated by using the average of the exchange rates on the last day of each month during the period, are set forth below:

	2015	2014	2013	2012	2011
Average 1 US $ = NIS	3.88	3.58	3.61	3.71	3.67

The high and low exchange rates for each month during the previous six months are set forth below:

	September 2015	October 2015	November 2015	December 2015	January 2016	February 2016
High 1 US $ = NIS	3.95	3.92	3.92	3.91	3.98	3.96

Low						
1 US $ = NIS	3.86	3.82	3.87	3.86	3.91	3.87

B. Capitalization and Indebtedness.

Not applicable.

C. Reasons for the Offer and Use of Proceeds.

Not applicable.

D. Risk Factors.

Risks Related to Our Financial Position and Capital Requirements

We are a clinical-stage biopharmaceutical company with a history of operating losses. We expect to incur significant additional losses in the future and may never be profitable.

We are a clinical-stage biopharmaceutical company with an operating history limited to clinical development of one product and no approved products. To date, we have focused nearly exclusively on developing our product candidate, Aramchol. We have funded our operations to date primarily through proceeds from the private placement of ordinary shares, convertible debt and our initial public offering on March 18, 2014. In addition, we have limited operating experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical industry. We currently have no products approved for marketing in the United States or any other jurisdiction and have not generated any revenue from product sales to date. We have incurred operating losses in each year since the inception of our predecessor in 2000. Our loss attributable to holders of our ordinary shares for the years ended December 31, 2014 and 2015 was approximately $9.1 million and $10.6 million, respectively. As of December 31, 2015, we had an accumulated deficit of $47.4 million. Substantially all of our operating losses resulted from costs incurred in connection with our development program and from general and administrative costs associated with our operations.

Our ability to become profitable depends upon our ability to generate revenue in excess of our expenses. To date, we have not generated any revenue as our lead product candidate, Aramchol, is still in clinical development and has not been approved by the FDA, nor has any other product candidate. We do not know when, or if, we will generate any revenue. We do not expect to generate revenue unless and until we, or an ultimate third-party licensor or acquirer, obtain regulatory and marketing approval of, and commercialize, Aramchol, or any other product candidate. We will continue to incur research and development and general and administrative expenses related to our operations. We expect to continue to incur losses for the foreseeable future, which may be significant, and these losses will likely increase as we:

- initiate and manage additional clinical trials for Aramchol, and initiate additional research and development programs;
- seek regulatory approvals for our product candidate, or future product candidates, if any;
- implement internal systems and infrastructures, including, without limitation, hiring of additional personnel as needed and developing sales and marketing functions if and when our product candidate receives applicable

regulatory approval;

- seek to in-license additional products or technologies to develop;
- hire additional management and other personnel; and
- move towards commercialization of our product candidate and future product candidates, if any.

We may out-license Aramchol before it is approved by any applicable regulatory agency, commercialized and/or generates revenue, depending on a number of factors, including our ability to:

- obtain favorable clinical results from and progress the clinical development of Aramchol;
- develop and obtain regulatory approvals in the countries and for the uses we intend to pursue for Aramchol;

- contract for the manufacture of commercial quantities of Aramchol by a cGMP compliant manufacturing facility at acceptable cost levels if marketing approval is received; and

- establish external, and potentially in the future, internal, sales and marketing capabilities to effectively market and sell Aramchol in the United States and other countries.

Even if Aramchol is approved for commercial sale for the treatment of NASH in OD patients, or for any other indications, it may not gain market acceptance or achieve commercial success. In addition, we anticipate incurring significant costs associated with seeking regulatory approval and commercialization. We may not achieve profitability soon after generating product revenue, if ever. If we are unable to generate product revenue, we will not become profitable and would be unable to continue operations without additional funding.

We expect our research and development expenses to increase in connection with our planned clinical trials and potential initiation of clinical trials for other indications. In addition, if we obtain marketing approval for Aramchol and opt to commercialize it ourselves, we will likely initially incur significant expenses associated with outsourcing sales, marketing and manufacturing functions to third parties, as well as continued research and development expenses. Furthermore, we expect to incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

Our limited operating history makes it difficult to evaluate our business and prospects.

Our operating history is limited to clinical development of one product, and our operations to date have been limited primarily to research and development, raising capital and recruiting scientific and management personnel and third-party partners. Therefore, it may be difficult to evaluate our business and prospects. We have not yet demonstrated an ability to commercialize or obtain regulatory approval for any product candidate. Consequently, any predictions about our future performance may not be accurate, and you may not be able to fully assess our ability to complete development and/or commercialize our product candidate, or any future product candidate, obtain regulatory approvals or achieve market acceptance or favorable pricing for our product candidate or any future product candidate.

We have not yet commercialized any products and we may never be able to do so, and even if we do, the products may not gain market acceptance.

We have not yet commercialized any products and we may never be able to do so. We do not know when or if we will complete any of our product development efforts, obtain regulatory approval for any product candidates or successfully commercialize any approved products. Even if we are successful in developing products that are approved for marketing, we will not be successful unless these products gain market acceptance for appropriate indications at favorable reimbursement rates. The degree of market acceptance for these products will depend on a number of factors, including:

- the timing and scope of regulatory approvals in the countries we intend to pursue with respect to the commercialization of our product candidates, including the indications for which they are approved;
- the competitive environment;
- the ability for our products to be manufactured, whether by us or third parties, in compliance with applicable regulatory requirements, including cGMP;
- our ability to effectively promote our products, whether directly or using third parties, consistent with the approved indications and labeling in the countries in which we intend to pursue approval;
- the acceptance by the medical community of the safety and clinical efficacy of our products and their potential advantages over other therapeutic products;

- the development of a non-invasive method for diagnosing NASH as an alternative to the current gold standard of liver biopsy, which we view as a rate-limiting factor to complete market uptake because of its expense and its risks and discomfort to patients;

- the adequacy and success of distribution, sales and marketing efforts, including through strategic agreements with pharmaceutical and biotechnology companies; and

- the pricing and reimbursement policies of government and third-party payors, such as insurance companies, health maintenance organizations and other plan administrators.

Physicians, patients, third-party payors or the medical community in general may be unwilling to accept, utilize or recommend, and in the case of third-party payors, cover any of our planned future products. As a result, we are unable to predict the extent of future losses or the time required to achieve profitability, if at all. Even if we successfully develop one or more products, we may not become profitable.

We will likely need substantial additional capital in the future. If additional capital is not available, we will have to delay, reduce or cease operations.

We currently estimate that our cash position will support our current clinical trials and operations into 2017. We will likely need to raise substantial additional capital to fund our operations and to develop Aramchol for, and beyond its current development stage for the NASH indication, as well as additional indications, and ultimately commercialize it, if we choose to do so, for NASH or any other indication. In addition, we may choose to expand our current research and development focus, or other clinical operations, which may also require additional capital. As of December 31, 2015, we had a net working capital of $20.8 million, cash and cash equivalents of $4.2 million and marketable securities of $18.8 million. Our future capital requirements may be substantial and will depend on many factors including:

- adhering to patient recruitment in the our ongoing ARREST Study, based on our current estimation;

- our clinical trial results;

- exploration of the possibility to develop Aramchol for the treatment of other conditions or indications beyond those being explored in the ARREST Study and the ARamchol for the Reversal of HIV-AssociatEd lipodystrophy and NAFLD (ARRIVE) Study, or possible label expansion of Aramchol once its approved, if at all, for the treatment of other conditions or indications;

- the cost of filing and prosecuting patent applications and the cost of defending our patents;
- the cost of prosecuting infringement actions against third parties;
- the cost, timing and outcomes of seeking marketing approval of Aramchol;
- the costs associated with commercializing Aramchol if we receive marketing approval, and choose to commercialize Aramchol ourselves, including the cost and timing of establishing external, and potentially in the future, internal, sales and marketing capabilities to market and sell Aramchol;
- subject to receipt of marketing approval, revenue received from sales of approved products, if any, in the future;
- the costs associated with any product liability or other lawsuits related to our future product candidates or products, if any;
- the costs associated with post-market compliance with regulatory requirements, and of addressing any allegations of non-compliance by regulatory authorities in countries where we plan to market and sell Aramchol;

- the demand for our products;
- the costs associated with developing and/or in-licensing other research and development programs;
- the expenses needed to attract and retain skilled personnel; and
- the costs associated with being a public company.

Based on our current operating plan, we anticipate that our existing resources will be sufficient to enable us to maintain our currently planned operations, including our continued product development, into 2017. We believe these funds will enable us to complete any preparatory clinical and non-clinical work, as well as our ARREST Study, assuming that we adhere to patient recruitment based on our current estimation. We will require significant additional funds to initiate and complete additional clinical trials, including but not limited to a possible Phase III pivotal trial for the treatment of OD patients with NASH, and the FDA and EMA approval processes. However, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, such as losing our Small and Medium Enterprise status at the EMA, which entitles us to significant fee reductions. Because there are numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amount of increased capital outlays and operating expenditures associated with our anticipated clinical trials. We have no committed external sources of funds. Additional financing may not be available when we need it or may not be available on terms that are favorable to us and additional financing may cause significant dilution to our existing shareholders. If adequate funds are not available to us on a timely basis, or at all, we may be required to terminate or delay planned or ongoing clinical trials or other development activities for Aramchol.

Raising additional capital may be costly or difficult to obtain and will dilute current shareholders' ownership interests.

Any debt or equity financing that we may need or desire may not be available on terms favorable to us, or at all. If we obtain funding through a strategic collaboration or licensing arrangement, we may be required to relinquish our rights to certain of our technologies, products or marketing territories. If we are unable to obtain required additional capital, we may have to curtail our growth plans or cut back on existing business, and we may not be able to continue operating if we do not generate sufficient revenues from operations needed to stay in business.

We may incur substantial costs in pursuing future capital financing, including investment banking fees, legal fees, accounting fees, securities law compliance fees, printing and distribution expenses and other costs. We may also be required to recognize non-cash expenses in connection with certain securities we issue, such as convertible notes and warrants, which may adversely impact our financial condition and results of operations.

Any additional capital raised through the sale of equity or equity-linked securities may dilute our current shareholders' ownership in us and could also result in a decrease in the market price of our ordinary shares. The terms of those securities issued by us in future capital transactions may be more favorable to new investors and may include the issuance of warrants or other derivative securities, which may have a further dilutive effect.

We are unable to estimate our long-term capital requirements due to uncertainties associated with the development and commercialization of our product candidate. If we fail to obtain necessary funds for our operations, we will be unable to maintain and improve our intellectual property and technology, and we will be unable to develop and commercialize our product candidate.

Our long-term capital requirements are expected to depend on many potential factors, including, among others:

- the number of product candidates in development;
- the size, duration and scope of existing and future clinical trials;

- the regulatory path of our lead product candidate;
- the results of our clinical trials, which can be unpredictable in product candidate development;
- our ability to successfully commercialize our product candidates, including securing commercialization and out-licensing agreements with third parties and favorable pricing and market share;
- the progress, success and cost of our clinical trials and research and development programs, including those associated with milestones and royalties;
- the costs, timing and outcome of regulatory review and obtaining regulatory approval of our lead product candidate and addressing regulatory and other issues that may arise post-approval;
- the breadth of the labeling, assuming that our product candidate is approved for commercialization by a relevant regulatory authority, which may not occur;
- our need, or decision, to acquire or in-license complementary technologies or new platform technologies or product candidates;
- the costs of enforcing our issued patents and defending intellectual property-related claims;
- the costs of investigating patents that might block us from developing potential product candidates;
- the costs of recruiting and retaining qualified personnel;
- the costs associated with contracting with third parties to manufacture the product and to perform other necessary services;
- our revenue, if any; and
- our consumption of available resources more rapidly than currently anticipated, resulting in the need for additional funding sooner than anticipated.

If we are unable to obtain the funds necessary for our operations, we will be unable to maintain and improve our intellectual property and technology, and we will be unable to develop and commercialize Aramchol, or other product

candidates, which would materially and adversely affect our business, liquidity and results of operations.

We may become subject to the payment of taxes in connection with the Reorganization.

On February 2, 2014, we underwent a reorganization, or the Reorganization, pursuant to which all of our current business (including our intellectual property) was transferred to us. The Reorganization was effected by way of share transfers and asset transfers, as follows: First, GHI, our predecessor, transferred the entire share capital of Galmed 2000 Inc., a holdings company incorporated in the British Virgin Islands, or GTTI, to the Company; next, GTTI transferred the entire share capital of Galmed International Limited, a company incorporated in Malta, a European Union, or EU, member state, or GIL, to the Company; then, GIL transferred and assigned all of its intellectual property to Galmed Research and Development Ltd., a newly formed Israeli company, or GRD. GIL held all of the equity rights in and to Galmed Medical Research Ltd., an Israeli company, or GMR. In connection with the Reorganization, we obtained a tax pre-ruling, or the Tax Pre-Ruling, from the Israeli Tax Authority. The Tax Pre-Ruling confirms that the transfer of shares and assets resulting in the Company as the parent company and 100% equity-owner of GRD, which holds all of the Group's intellectual property, including the Company's patent portfolio, GIL and GTTI, is not taxable pursuant to the provisions of Sections 131 and 132 of the Income Tax Ordinance (New Version) — 1961, or the Israeli Tax Ordinance, as long as certain requirements are met. However, we have not obtained a tax pre-ruling from the tax authorities in the British Virgin Islands with respect to the transfer of the shares of GTTI and the transfer of the shares of GIL to the Company, or from the tax authorities in Malta with respect to the transfer of the intellectual property of GIL to GRD. We believe that such transfers of shares and assets are not taxable in the British Virgin Islands and Malta, respectively. However, there can be no assurance that we will not become subject to the payment of taxes in the British Virgin Islands, with respect to the transfers of shares as aforesaid, or in Malta, in connection with the transfer of the intellectual property as mentioned above. See also "Item 4. Information on the Company—Historical Background and Corporate Structure" below.

Risks Related to Our Business, Industry and Regulatory Requirements

We depend largely on the success of our product candidate, Aramchol, and we may not obtain regulatory approval of Aramchol.

We have invested almost all of our efforts and financial resources in the research and development of Aramchol, which is currently our only product candidate. As a result, our business is largely dependent on our ability to complete the development of, obtain regulatory approval for and successfully commercialize Aramchol in a timely manner. The process to develop, obtain regulatory approval for and commercialize Aramchol is long, complex, costly and uncertain as to its outcome.

The research, testing, clinical trials, manufacturing, labeling, approval, sale, marketing and distribution of drugs are subject to extensive regulation by the FDA and other regulatory agencies in other countries. These regulations differ from jurisdiction to jurisdiction. We have not received marketing approval for Aramchol in any jurisdiction. We are not permitted to market Aramchol, or any other product candidate, in the United States until we receive approval of a New Drug Application, or NDA, from the FDA, or in any foreign countries until we receive the requisite approval from the respective regulatory agencies in such countries. We are currently in the midst of conducting the Phase IIB ARREST Study and have not yet begun any pivotal study of Aramchol, We have not received regulatory authorization to conduct the clinical trials that are necessary to file an NDA with the FDA or comparable applications to other regulatory authorities in other countries. The results of clinical trials may be unsatisfactory, and even if we believe those clinical trials to be successful, the FDA, or other regulatory authorities, may not grant marketing authorization should we be in a position to request it.

The requirements and length of time for approval vary in different jurisdictions and could involve additional studies of Aramchol beyond those we currently anticipate. The time required to obtain approval in other countries might differ from that required to obtain FDA approval in the United States. The marketing approval process in other countries may include all of the risks detailed above regarding FDA approval as well as other risks. In particular, in many countries outside the United States, it is required that a product receive pricing and reimbursement approval before the product can be commercialized. This can result in substantial delays in such countries. In other countries, product approval depends on showing superiority to an approved therapy. This can result in significant expense to conduct complex clinical trials. Finally, we do not have any products approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

Marketing approval in one jurisdiction does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the regulatory process in others.

Failure to obtain marketing approval in other countries or any delay or setback in obtaining such approval would impair our ability to develop foreign markets for Aramchol. This would reduce our target market and limit the full commercial potential of Aramchol.

We may be forced to abandon development of Aramchol, or other future product candidates, which will significantly impair our ability to generate product revenues.

Upon the completion of any clinical trial, the results might not support the desired indications for use. Further, success in earlier clinical trials does not ensure that later clinical trials will be successful, and the results of later clinical trials may not replicate the results of prior clinical trials or preclinical testing. The clinical trial process may fail to demonstrate that Aramchol is safe and effective for the indications we seek. Any such failure may cause us to abandon Aramchol and may delay development of other product candidates. Any delay in, or termination or suspension of, our clinical trials will delay the requisite filings with the FDA or other regulatory agencies and, ultimately, our ability to commercialize our product candidates and generate product revenues. If the clinical trials do not support our desired indications, the completion of development of such product candidate may be significantly delayed or abandoned, which will significantly impair our ability to generate revenues and will materially adversely affect our results of operations.

If we acquire or in-license additional technologies or product candidates, we may incur a number of costs, may have integration difficulties and may experience other risks that could harm our business and results of operations.

We may acquire or in-license additional product candidates and technologies. Any product candidate or technologies we in-license or acquire will likely require additional development efforts prior to commercial sale, including extensive preclinical or clinical testing, or both, and approval by the FDA and applicable foreign regulatory authorities, if any. All product candidates are prone to risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate, or product developed based on in-licensed technology, will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure that any product candidate that we develop based on acquired or in-licensed technology that is granted regulatory approval will be manufactured or produced economically, successfully commercialized or widely accepted or competitive in the marketplace. Moreover, integrating any newly acquired or in-licensed product candidates could be expensive and time-consuming. If we cannot effectively manage these aspects of our business strategy, our business may not succeed.

The clinical trial process is complex and expensive, and commencement and completion of clinical trials can be delayed or prevented for a number of reasons.

We may not be able to complete or commence the clinical trials that would support our submission of an NDA to the FDA, a Marketing Authorization Application, or MAA, to the EMA or any similar submission to regulatory authorities in other countries. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. The fact that the FDA, EMA or other regulatory authorities permit a company to conduct human clinical trials is no guarantee that the trials will be successful. On the contrary, most candidate drugs that begin clinical trials do not prove to be successful and do not result in the filing of an NDA, MAA or similar filing. Drug candidates that successfully complete one phase of clinical trials may prove unsuccessful at a subsequent phase. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements and in part because the results of clinical trials are inherently uncertain and unpredictable. Regulatory authorities, such as the FDA, may decline to permit a clinical trial to proceed or may suspend a clinical trial that it has previously permitted to proceed. Additionally, the clinical trial process is time-consuming, and failure can occur at any stage of the trials. We may encounter problems that cause us to abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed by several factors, including:

- difficulties obtaining regulatory authorization to commence a clinical trial or complying with regulatory requirements for clinical trials or with the conditions imposed by a regulatory authority regarding the scope or duration of a clinical trial;

- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among

different CROs and trial sites;

- insufficient or inadequate supply or quality of a product candidate or other materials necessary to conduct our clinical trials;

- difficulties in obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;

- delays resulting from a decision of the FDA not to designate Aramchol as a Breakthrough Therapy, a designation that could, among other benefits, expedite the conduct of clinical trials;

- challenges in recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including size and nature of patient population, proximity of patients to clinical sites, eligibility and exclusion criteria for the trial, nature of trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications.

The ARREST Study may also be delayed or terminated as a result of, but not limited to, inadequate recruitment rate or speed thereof or safety signals. In addition, the ARREST Study or other clinical trials may be suspended or terminated by us, the FDA or other regulatory authorities, the principal investigator at a site, the IRBs at the sites where such boards are overseeing a trial or the data safety monitoring board, or DSMB, that is overseeing the clinical trial at issue, or other regulatory authorities due to a number of factors, including:

- irregularities in conducting a clinical trial, including by way of example, failure to conduct the clinical trial in accordance with regulatory requirements, in particular good clinical practice requirements, or GCP, or the FDA-authorized clinical protocols;

- negative findings upon inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities;

- unforeseen safety issues or lack of effectiveness; and

- lack of adequate funding to continue the clinical trials.

To date, we have already experienced material delays in the ARREST Study largely related to slower than expected recruitment and the length of time required to obtain regulatory authorizations to proceed with clinical trials, as well as the termination of a Phase IIA trial of Aramchol for the treatment and dissolution of cholesterol gallstones. We may experience further delays, and there can be no assurance that we will not experience such risks in the future as we progress with our planned clinical trials.

Furthermore, positive results in previous clinical studies of Aramchol may not be predictive of similar results in future clinical trials. Also, interim results, if at all, during a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage development. Accordingly, the results from the completed preclinical studies and clinical trials for Aramchol may not be predictive of the results we may obtain in later stage trials. Our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical and clinical studies have nonetheless failed to obtain FDA or EMA, or other regulatory agency, approval for their products.

In addition, we or regulatory authorities may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the regulatory authorities find deficiencies in our regulatory submissions or the conduct of such trials. Any suspension of clinical trials will delay possible regulatory approval, if any, and adversely impact our ability to develop products and generate revenue.

The lack of a reliable non-invasive method for the diagnosis of NASH is likely to present a major challenge to our product candidate's market penetration, if ever commercialized.

Liver biopsy is the standard approach for the diagnosis of inflammation and fibrosis associated with NASH. However, the procedure-related morbidity, sample errors, costs, patient discomfort and thus lack of patient interest in undergoing the procedure limit its use. As such, only patients with a high risk of NASH, which includes patients with metabolic syndrome and an indication of Non-Alcoholic Fatty Liver Disease, or NAFLD, are generally sent for liver biopsy. Because NASH tends to be asymptomatic until the disease progresses, many individuals with NASH go undiagnosed until the disease has reached its late stages. The lack of a reliable non-invasive method for the diagnosis of NASH is likely to present a major challenge to Aramchol's market penetration, as many practitioners and patients may not be aware that a patient suffers from NASH and requires treatment. As such, use of Aramchol might not be as wide-spread as our actual target market and this may limit the commercial potential of Aramchol.

A further challenge to Aramchol's market penetration is that currently a liver biopsy is the standard approach for measuring improvement in NASH patients. Because it would be impractical to subject all Aramchol users to regular and repeated liver biopsies, it will be difficult to demonstrate Aramchol's effectiveness to practitioners and patients unless and until a reliable non-invasive method for the diagnosis and monitoring of NASH becomes available, as to which there can be no assurance.

While we, and other companies in the industry, are currently working on advancing non-invasive diagnostic approaches, none of these has been clinically validated, and the timetable for commercial validation, if at all, is uncertain. Moreover, such diagnostics may also be subject to regulation by FDA or other regulatory authorities as medical devices and may require premarket clearance or approval.

Obtaining approval of an NDA, or other regulatory approval, even after clinical trials that are believed to be successful, is an uncertain process.

Even if we complete our planned clinical trials and believe that the clinical data confirms that the drug is both safe and effective for its intended use, obtaining approval of an NDA, or similar regulatory application, is an extensive, lengthy, expensive and uncertain process, and the FDA and other regulatory agencies may delay, limit or deny approval of Aramchol for many reasons, including, without limitation, the fact that:

- we may not be able to demonstrate to the satisfaction of the applicable regulatory agencies that Aramchol is safe and effective for treatment of NASH in OD patients or for any other indication;
- the results of clinical trials may not meet the level of statistical significance or clinical significance required by the applicable regulatory agencies for approval;
- the applicable regulatory agencies may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the applicable regulatory agencies may not find the data from preclinical studies and clinical trials sufficient to demonstrate that Aramchol's clinical and other benefits outweigh its safety risks;
- the applicable regulatory agencies may disagree with our interpretation of data from preclinical studies or clinical trials;
- the applicable regulatory agencies may not accept data generated at our clinical trial sites;

- the data collected from preclinical studies and clinical trials of Aramchol may not be sufficient to support the submission of an NDA or similar regulatory application;

- the applicable regulatory agencies may not schedule an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the applicable regulatory agencies require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;

- the applicable regulatory agencies may require development of a risk evaluation and mitigation strategy, or REMS, as a condition of approval;

- the applicable regulatory agencies may require simultaneous approval for both adults and children, which would delay required approvals, or we may have successful clinical trial results for adults, but not children, or vice versa;

- the applicable regulatory agencies may change their approval policies or adopt new regulations that may impede consideration or approval of our NDA, or similar regulatory application;

- the applicable regulatory agencies may identify deficiencies in the manufacturing processes or facilities of third-party manufacturers, or suppliers of active pharmaceutical ingredients, or APIs, with which we enter into agreements for clinical and commercial supplies; and

- the applicable regulatory agencies may require post-marketing approval studies, such as Phase IV clinical trials, in connection with Aramchol.

Before we can submit an NDA to the FDA or a similar approval application to other regulatory authorities, as applicable, we must complete the ongoing ARREST Study and conduct one or more Phase III clinical trials that will be substantially broader than our Phase IIB trial. We will also need to agree on a protocol with the FDA for any Phase III clinical trial before commencing that trial in the United States. Clinical trials frequently produce unsatisfactory results even though prior clinical trials were successful. Therefore, the results of the Phase IIB or Phase III clinical trials that we conduct may or may not be successful. The applicable regulatory agencies may suspend all clinical trials or require that we conduct additional clinical, nonclinical, manufacturing, validation or drug product quality studies and submit data from these additional studies before considering or reconsidering the NDA or similar regulatory application. Depending on the extent of these, or any other studies, approval of any applications that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the applicable regulatory agencies to provide regulatory approval. If any of these outcomes occur, we would not receive approval for Aramchol and may be forced to cease operations.

Even if we obtain regulatory approval for Aramchol, the approval might contain significant limitations related to the indications for use for which the drug is approved, use restrictions including, without limitation, for certain labeled populations, age groups, warnings, precautions or contraindications, or may be subject to significant post-marketing studies or risk mitigation requirements. If we are unable to successfully commercialize Aramchol, we may be forced to cease operations.

Aramchol may produce undesirable side effects that we may not detect in our clinical trials, which could prevent us from achieving or maintaining market acceptance of this product candidate and could substantially increase commercialization costs or even force us to cease operations.

Even if Aramchol receives marketing approval, we or others may later identify undesirable side effects caused by the product. In that event, regulatory authorities may:

- suspend or withdraw their approval of the product;

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require the addition of labeling statements, such as warnings, so-called “black box warnings,” contraindications or restrictions on the product’s intended use;

- require us to issue specific communications to healthcare professionals, such as “Dear Doctor” letters;

- issue negative publicity regarding the affected product, including safety communications;

- impose a risk evaluation and mitigation strategy (REMS), in the case of FDA, or similar risk management strategies in the case of foreign regulators;

In addition to these potentially significant negative consequences, we could be required to change the way the product is administered, conduct additional preclinical studies or clinical trials or restrict or cease the distribution or use of the product, and/or be sued and held liable for harm caused to patients. The foregoing or other events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase commercialization costs or even force us to cease operations.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, patient willingness to undergo a liver biopsy in our NASH trials, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and disadvantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Potential patients for Aramchol may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our studies.

We will be required to identify and enroll a sufficient number of patients in the U.S. with NASH for each of our ongoing and planned clinical trials of Aramchol in this indication. We also may encounter difficulties in identifying and enrolling U.S. NASH patients who meet the eligibility criteria for our planned clinical trials. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible patients to participate in the clinical trials required by the FDA or other foreign regulatory agencies. In addition, the process of finding and diagnosing patients may prove costly. Our inability to enroll a sufficient number of patients for any of our clinical trials would result in significant delays or may require us to abandon one or more clinical trials.

Changes in regulatory requirements and guidance or unanticipated events during our clinical trials may occur, which may result in necessary changes to clinical trial protocols, which could result in increased costs to us, delay our development timeline or reduce the likelihood of successful completion of our clinical trials.

Changes in regulatory requirements or guidance or unanticipated events during our clinical trials may result in the need for us to amend clinical trial protocols. Amendments may require review and approval by regulators and/or IRBs, and re-consent subjects, which may adversely affect the cost, timing or successful completion of a clinical trial. If we experience delays in the completion of, or if we terminate, any of our clinical trials, the commercial prospects for Aramchol would be harmed and our ability to generate product revenue would be delayed, possibly materially.

We cannot be certain that the results of our potential Phase III clinical trials, even if all endpoints are met, will support definitive regulatory approval of Aramchol for the treatment of NASH in OD patients.

Further, specific to us, a number of issues still remain unclear with regard to the potential Phase III protocol, including, among other issues, the (i) duration of study, (ii) number of subjects required, (iii) dosages, and (iv) approvable endpoints. These factors, among others, would play a material role in determining the cost of such study(ies) and ultimate probability of success.

Even if Aramchol, or any other product candidate that we may develop, receives marketing approval, we will continue to face extensive regulatory requirements and any such product may still face future regulatory risks or new requirements.

Even if we receive regulatory approval to market a particular product candidate, any such product will remain subject to extensive regulatory requirements, including requirements relating to manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, distribution and recordkeeping. Even if regulatory approval of a product is granted, the approval may be subject to limitations on the uses for which the product may be marketed or the conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, which could negatively affect us by reducing revenues or increasing expenses, and cause the approved product candidate not to be commercially viable. In addition, as clinical experience with a drug expands after approval, typically because it is used by a greater number and more diverse group of patients after approval than during clinical trials, side effects and other problems may be observed over time after approval that were not seen or anticipated during pre-approval studies. Any adverse effects observed after the approval and marketing of a product candidate could result in limitations on the use of the approved product, withdrawal of FDA approval of the previously approved product, or voluntary withdrawal from the marketplace of the approved product. Absence of long-term safety data may also limit the approved uses of our products, if any. If we fail to comply with the regulatory requirements of the FDA, and other applicable U.S. and foreign regulatory authorities, or previously unknown problems with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks, including the following:

- suspension or imposition of restrictions on operations, including costly new manufacturing requirements;
- refusal to approve pending applications or supplements to applications;
- suspension of any ongoing clinical trials;
- suspension or withdrawal of marketing approval;
- an injunction or imposition of civil or criminal penalties or monetary fines;
- seizure or detainment of products;
- banning or restriction of imports and exports;
- issuance of warning letters or untitled letters;
- suspension or imposition of restrictions on operations, including costly new manufacturing requirements; or
- refusal to approve pending applications or supplements to applications.

In addition, various aspects of our operations are subject to federal, state or local laws, rules and regulations, any of which may change from time to time. Costs arising out of any regulatory developments could be time-consuming and expensive and could divert management resources and attention and, consequently, could adversely affect our business operations and financial performance.

Delays in regulatory approval, limitations in regulatory approval and withdrawals of regulatory approval may have a material adverse effect on the Company. If we experience significant delays in testing or receiving approvals or sign-offs to conduct clinical trials, our product development costs will increase and our ability to out-license product candidates may be impeded.

If we obtain approval to commercialize Aramchol outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If Aramchol is approved for commercialization outside the United States, we will likely enter into agreements with third parties to commercialize Aramchol outside the United States. We expect that we will be subject to additional risks related to entering into or maintaining international business relationships, including, without limitation:

- different regulatory requirements for drug approvals in foreign countries;
- differing U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;

- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors;
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters; and
- risks associated with clinical co-development agreements in other jurisdictions prior to or post-regulatory approval.

A failure to timely and effectively address the additional risks related to entering into or maintaining international business relationships could have a material adverse effect on our business, liquidity operating results and financial condition.

If we receive marketing approval for Aramchol, sales will be limited unless the product achieves broad market acceptance.

The commercial success of Aramchol and any other future product candidate for which we obtain marketing approval from the FDA, or other regulatory authorities, will depend on the breadth of its approved labeling and upon the acceptance of the product by the medical community, including physicians, patients and healthcare payors. The degree of market acceptance of any approved product will depend on a number of factors, including, without limitation:

- demonstration of clinical safety and efficacy compared to other products;
- ability of physicians to accurately diagnose NASH in its early stages;
- the relative convenience and ease of administration;

- the prevalence and severity of any adverse side effects;
- limitations, warnings or contraindications contained in the product's approved labeling;
- distribution and use restrictions imposed by the FDA, or other regulatory agencies, or agreed to by us as part of a mandatory or voluntary REMS;
- availability of alternative treatments, including, in the case of Aramchol, a number of competitive products already approved or expected to be commercially launched in the near future;
- pricing and cost effectiveness;
- the effectiveness of our, or any future collaborators', sales and marketing strategies;
- our ability to obtain sufficient third-party coverage or reimbursement; and
- the willingness of patients to pay for drugs out of pocket in the absence of third-party coverage.

If Aramchol is approved, but does not achieve an adequate level of acceptance by physicians, healthcare payors and patients, we may not generate sufficient revenue from the product, and we may not become profitable. In addition, our efforts to educate the medical community and third-party payors on the benefits of the product may require significant resources and may never be successful.

Maintaining our reputation and brand image is essential to our business success.

Our success in maintaining, extending and expanding our brand image depends on our ability to adapt to a rapidly changing media environment, including our increasing reliance on social media, such as the Company's website, Twitter, Facebook and LinkedIn, and online dissemination of advertising campaigns. We are subject to a variety of legal and regulatory restrictions on how and to whom we market our product candidate, Aramchol. These restrictions may limit our ability to maintain, extend and expand our brand image as the media and communications environment continues to evolve. Negative posts or comments about us on social networking web sites could seriously damage our reputation and brand image. If we do not maintain, extend and expand our brand image, then our product sales, financial condition and results of operations could be materially and adversely affected.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are inconsistent with the FDA-approved indications and other conditions or restrictions contained in the approved labeling, including the prescribing information, for the product. In particular, any labeling approved by FDA or other foreign regulatory agencies for Aramchol necessarily limits its use for certain conditions in certain patient populations. Also, regulatory agencies may impose further requirements or restrictions on the distribution or use of Aramchol as part of a mandatory plan, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. If we receive marketing approval for Aramchol, physicians may nevertheless prescribe Aramchol to their patients in a manner that is inconsistent with the approved labeling, which is commonly known as "off label" use. If we are found to have promoted our products for such "off label" uses, we may become subject to significant liability under a variety of statutory theories typically alleged by U.S. regulatory authorities. In particular, the U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion, has enjoined several companies from engaging in off-label promotion, and has requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

We may be subject to extensive environmental, health and safety, and other laws and regulations in multiple jurisdictions.

Our business involves the controlled use, through our service providers, of hazardous materials, various biological compounds and chemicals, and as such, we, our agents and our service providers may be subject to various environmental, health and safety laws and regulations, including those governing air emissions, water and wastewater discharges, noise emissions, the use, management and disposal of hazardous, radioactive and biological materials and wastes and the cleanup of contaminated sites. The risk of accidental contamination or injury from these materials cannot be eliminated. If an accident, spill or release of any regulated chemicals or substances occurs, we could be held liable for resulting damages, including for investigation, remediation and monitoring of the contamination, including natural resource damages, the costs of which could be substantial. We may incur substantial capital costs and operating expenses and may be required to obtain consents to comply with any environmental and health laws or regulations and the terms and conditions of any permits required pursuant to such laws and regulations, including costs incurred by us to install new or updated pollution control equipment for our service providers, modify our operations or perform other corrective actions at our facilities or the facilities of our service providers. In addition, fines and penalties may be imposed on us, our agents and/or our service providers for noncompliance with environmental, health and safety and other laws and regulations or for the failure to have, or comply with the terms and conditions of, required environmental or other permits or consents.

We expect the healthcare industry to face increased limitations on reimbursement, rebates and other payments as a result of healthcare reform, which could adversely affect third-party coverage of our products and how much or under what circumstances healthcare providers will prescribe or administer our products.

In both the United States and other countries, sales of our products will depend in part upon the availability of reimbursement from third-party payors, which include governmental authorities, managed care organizations and other private health insurers. Third-party payors are increasingly challenging the price and examining the cost effectiveness of medical products and services.

Increasing expenditures for healthcare have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would effect changes in the U.S. healthcare system have been introduced or proposed in U.S. Congress, or Congress, and in some state legislatures, including reducing reimbursement for prescription products and reducing the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Modernization Act, changed the way Medicare covers and pays for most pharmaceutical products in a number of ways. Medicare is the single largest third-party payment program and is administered by the Centers for Medicare & Medicaid Services, or CMS. Medicare traditionally covered prescription drugs administered by physicians. The Modernization Act introduced a new reimbursement methodology based on average sales prices for many of these drugs. The Modernization Act also established a new competitive acquisition program for the purchase of Part B drugs. This program, when fully implemented, will likely reduce the prices of these drugs. While the Medicare provisions of the Modernization Act apply only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payors.

Most notably, the Modernization Act also expanded coverage through a new Part D to include ordinary self-administered outpatient drugs. Medicare part D though operates through private insurers, and these insurers negotiate prices with pharmacies and with manufacturers. Intense negotiations can result in reduced revenues to manufacturers.

Increasing expenditures for healthcare have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would effect changes in the U.S. healthcare system have been introduced or proposed in U.S. Congress, or Congress, and in some state legislatures, including reducing reimbursement for prescription products and reducing the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010, or the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. The Affordable Care Act expanded manufacturers' Medicaid rebate liability to include covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, increased the minimum rebate due for innovator drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP. The rebate on innovator drugs is the greater of 23.1% of the AMP per unit or the difference between the AMP and the best price per unit and adjusted by the Consumer Price Index-Urban (CPI-U) based on a launch date and current quarter AMP. The total rebate amount for innovator drugs is capped at 100.0% of AMP. The Affordable Care Act and subsequent legislation also narrowed the definition of AMP. Furthermore, the Affordable Care Act imposes a significant annual, nondeductible fee on companies that manufacture or import certain branded prescription drug products. Substantial new provisions affecting compliance were also been enacted, which may affect our business practices with healthcare practitioners. Although it is too early to determine the effect of the Affordable Care Act, it appears likely to continue to put pressure on pharmaceutical pricing, especially under the Medicare and Medicaid programs, and may also increase our regulatory burdens and operating costs.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. More recently, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of an amount greater than $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, starting in 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several categories of healthcare providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. If we ever obtain regulatory approval and commercialization of Aramchol, these new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of Aramchol may be. Further, the Deficit Reduction Act of 2010, directed CMS to contract a vendor to determine "retail survey prices for covered outpatient drugs that represent a nationwide average of consumer purchase prices for such drugs, net of all discounts and rebates (to the extent any information with respect to such discounts and rebates is available)." This survey information can be used to determine the National Average Drug Acquisition Cost, or NADAC. Some states have indicated that they will reimburse based on the NADAC and this can result in further reductions in the prices paid for various outpatient drugs.

Although we cannot predict the full effect on our business of the implementation of existing legislation or the enactment of additional legislation pursuant to healthcare and other legislative reform, we believe that legislation or regulations that would reduce reimbursement for, or restrict coverage of, our products could adversely affect how much or under what circumstances healthcare providers will prescribe or administer our products. This could materially and adversely affect our business by reducing our ability to generate revenue, raise capital, obtain additional collaborators and market our products. In addition, we believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of pharmaceutical products, which may adversely impact product sales.

It will be difficult for us to profitably sell Aramchol if reimbursement for the product is limited by government authorities and third-party payor policies.

In addition to any healthcare reform measures that may affect reimbursement, the market acceptance and sales of Aramchol will depend on the reimbursement policies of government authorities and third-party payors. It will be difficult for us to profitably sell Aramchol if reimbursement for the product is limited by government authorities or third-party payors. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage or reimbursement will be available for Aramchol and, if coverage and

reimbursement are available, of the extent of coverage and the level of reimbursement. Reimbursement may affect the demand for, or the price of, any product for which we obtain marketing approval. In addition, third-party payors are likely to impose strict requirements for reimbursement in order to limit off-label use of a higher priced drug. Reimbursement by a third-party payor may depend upon a number of factors including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

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Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for our future products. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our future products. If reimbursement is not available, or is available only to limited levels, we may not be able to commercialize our product candidate, or any future product candidates, profitably, or at all, even if approved. In addition, if physicians, government agencies and other third-party payors do not accept the use or efficacy of Aramchol, we will not be able to generate significant revenue, if any.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

We are subject to federal anti-kickback laws and regulations. Our failure to comply with these laws and regulations could have adverse consequences to us.

There are extensive U.S. federal and state laws and regulations prohibiting fraud and abuse in the healthcare industry that can result in significant criminal and civil penalties. These federal laws include: The anti-kickback statute, which prohibits certain business practices and relationships, including the payment or receipt of remuneration for the referral of patients whose care will be paid by Medicare or other federal healthcare programs; the physician self-referral prohibition, commonly referred to as the Stark Law; the anti-inducement law, which prohibits providers from offering anything to a Medicare or Medicaid beneficiary to induce that beneficiary to use items or services covered by either program; the False Claims Act, which prohibits any person from knowingly presenting or causing to be presented false or fraudulent claims for payment by the federal government, including the Medicare and Medicaid programs; and the Civil Monetary Penalties Law, which authorizes the U.S. Department of Health and Human Services to impose civil penalties administratively for fraudulent or abusive acts. In addition, the Affordable Care Act requires drug manufacturers to report to the government any payments to physicians and certain hospitals for consulting services and the like.

Sanctions for violating these federal laws include criminal and civil penalties that range from punitive sanctions, damage assessments, monetary penalties, imprisonment, denial of Medicare and Medicaid payments or exclusion

from the Medicare and Medicaid programs, or both, and debarment. As federal and state budget pressures continue, federal and state administrative agencies may also continue to escalate investigation and enforcement efforts to root out waste and to control fraud and abuse in governmental healthcare programs. Private enforcement of healthcare fraud has also increased, due in large part to amendments to the civil False Claims Act in 1986 and again in 2009 and 2010 that were designed to encourage private persons to sue on behalf of the government. A violation of any of these federal and state fraud and abuse laws and regulations could have a material adverse effect on our liquidity and financial condition. An investigation into the use by physicians of any of our products, once commercialized, may dissuade physicians from either purchasing or using them, and could have a material adverse effect on our ability to commercialize those products.

If we or our manufacturers fail to comply with manufacturing regulations, our financial results and financial condition could be adversely affected.

Before an NDA is approved, and before we begin the commercial manufacture of Aramchol, contract manufacturers must register with FDA or foreign regulators undergo regulatory inspection of their manufacturing facilities, processes and quality systems. In addition, pharmaceutical manufacturing facilities are subject to periodic inspection by the FDA and foreign regulatory authorities after product approval. Due to the complexity of the processes used to manufacture pharmaceutical products and product candidates, any potential third-party manufacturer may be unable to meet local, federal, or international regulatory requirements either at the outset or on an ongoing basis, in a cost effective manner, if at all.

We do not intend to engage in the manufacture of our products other than for preclinical and clinical studies, but we or our materials suppliers may face manufacturing or quality control problems causing product production and shipment delays or a situation where we or the supplier may not be able to maintain compliance with the FDA's or foreign regulators' requirements necessary to continue manufacturing our product candidate. Drug manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding foreign regulators to ensure continuing compliance with applicable requirements. Any failure to comply with FDA or foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop and market our product candidate and any future product candidates.

If a third-party manufacturer with whom we contract is unable to comply with manufacturing requirements, we may be subject to fines, unanticipated compliance expenses, recall or seizure of our products, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions could adversely affect our financial results and financial condition.

Our market is subject to intense competition. If we are unable to compete effectively, Aramchol or any other product candidate that we develop may be rendered noncompetitive or obsolete.

There are a number of products in development for NASH in OD patients, many of which are being developed by pharmaceutical companies that are far larger than us, with significantly greater resources and more experience than us. Further, our industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large, fully-integrated pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. All of these competitors currently engage in, have engaged in or may engage in the future in the development, manufacturing, marketing and commercialization of new pharmaceuticals, some of which may compete with Aramchol or other product candidates. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. These companies may have products in development that are superior to Aramchol. Key competitive factors affecting the commercial success of Aramchol and any other product candidates that we develop are likely to be efficacy, time of onset, safety and tolerability profile, reliability, convenience of dosing, price and reimbursement.

Many of our potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drug candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than us in obtaining FDA and other marketing approvals for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render Aramchol or any other product candidates that we develop obsolete or non-competitive before we can recover the expenses of developing and commercializing the product. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render Aramchol, or any other product candidate that we develop, non-competitive or obsolete. If we cannot successfully

compete with new or existing products, our marketing and sales will suffer and we may never be profitable.

Our competitors currently include companies with marketed products and/or an advanced research and development pipeline. The majority of competitors in the liver disease therapeutic field include Intercept Pharmaceuticals, Inc., Genfit S.A., Gilead Sciences, Inc. and Tobira Therapeutics, Inc., among others. See also “Item 4. Information on the Company—Competition.” Moreover, several companies have reported the commencement of research projects and proof-of-concept trials related to NASH, including those mentioned in the preceding sentence. However, we are not aware if such projects are ongoing or have been completed and, to the best of our knowledge, there is no approved drug currently on the market which is similar to Aramchol, nor are we aware of any product candidate targeting NASH using a compound similar to Aramchol with respect to chemical profile and mechanism of action.

We face potential product and other liability exposure, and, if claims are brought against us, we may incur substantial liability.

Our products and product candidates could cause adverse events. These adverse events may not be observed in clinical trials, but may nonetheless occur in the future. If any of these adverse events occur, they may render our product candidates ineffective or harmful in some patients, and our sales would suffer, materially adversely affecting our business, financial conditions and results of operations.

In addition, potential adverse events caused by our product candidates, or products, could lead to product liability claims. Product liability claims might be brought against us by consumers, healthcare providers or others coming into contact with our products. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- decreased demand for Aramchol or any other product candidate for which we obtain marketing approval;
- impairment of our business reputation and exposure to adverse publicity;
- increased warnings on product labels or other regulatory actions;
- withdrawal of clinical trial participants;
- costs of related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- loss of revenue; and
- the inability to successfully commercialize Aramchol or any other product candidate for which we obtain marketing approval.

To date, no serious adverse events related to the study drug have been reported in any of our clinical studies, in which subjects have been administered doses up to 900 mg, at doses up to 600 mg administered once-daily for up to ten days and at doses up to 300 mg administered once-daily for up to three months. Several non-serious adverse events were reported in four completed and fully analyzed clinical trials. Those four studies enrolled a combined total of 168 patients.

In our Phase IA clinical trial we enrolled 17 healthy volunteers. A total of 34 adverse events were reported in nine subjects. All adverse events were mild or moderate and transient and resolved without sequelae. There were no serious adverse events, deaths or other significant adverse events observed in this study.

In our Phase IB placebo-controlled clinical trial with 25 healthy and mildly overweight male volunteers a total of 64 adverse events were reported by 80% of the subjects. A higher proportion of patients reported drug-related adverse events in the placebo group (88.9%) compared to the 30 mg active group (55.6%) and the 300 mg active group (71.4%). All adverse events were mild or moderate and resolved without sequelae. There were no serious adverse events, deaths or other significant adverse events.

We completed a pharmacokinetic, or PK, and food effect study in 66 healthy male volunteers consisting of three parts. Overall, over the three parts of the study, the vast majority of adverse events were mild and determined to be unrelated to Aramchol and all of the adverse events were transient and gave no indication of target organ toxicity. No serious adverse events or deaths occurred during the study. No clinically significant abnormalities related to any Aramchol dose were noted in electrocardiograms, or ECGs, laboratory results, vital signs or physical examinations.

In our Phase IIA placebo-controlled trial with 60 subjects with steatosis due to NAFLD or NASH, most adverse events were mild and transient, except for three (mild asthenia, mild nausea and moderate back pain), which were initially considered to be related to the study drug; however, after un-blinding the study results it was found that the three adverse events occurred in the placebo group. There was one serious adverse event reported, acute appendicitis, that was unrelated to study drug, which occurred in a patient taking the placebo. The patient fully recovered from the serious adverse event without sequelae and completed the study treatment. There were no deaths or other significant adverse events reported in this study.

If we are unable to obtain adequate insurance with respect to our clinical trials against and from any losses or claims from third parties, our financial condition could be adversely affected in the event of uninsured or inadequately insured loss or damage. We may not be able to obtain insurance policies on terms affordable to us that would adequately cover loss or claims by third parties. To the extent our business suffers any losses or claims by third parties, which are not covered, or adequately covered, by insurance, our financial condition may be materially adversely affected.

If product liability lawsuits are successfully brought against us, our insurance may be inadequate.

We have obtained insurance coverage for our clinical trials in accordance with market standards and in compliance with applicable Israeli law. However, our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for Aramchol, or any other product candidate, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial. A successful product liability claim, or series of claims, brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

The product liability insurance we will need to obtain in connection with the commercial sales of our product candidates, if and when they receive regulatory approval, may be unavailable in meaningful amounts or at a reasonable cost. If we are the subject of a successful product liability claim that exceeds the limits of any insurance coverage we obtain, we would incur substantial charges that would adversely affect our earnings and require the commitment of capital resources that might otherwise be available for the development and commercial launch of our product programs.

We manage our business through a small number of senior executive officers. We depend on them even more than similarly- situated companies.

Our future growth and success depends on our ability to recruit, retain, manage and motivate our senior executive officers. The loss of the services of our corporate officers, including President and Chief Executive Officer, Chief Medical Officer, Chief Financial Officer, Vice President of Clinical Operations, and Vice President of Drug Development, or the inability to hire or retain experienced management personnel, could adversely affect our ability to execute our business plan and harm our operating results.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified senior executive officers with scientific and technical experience. In particular, the loss of one or more of our senior executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We do not currently carry “key person” insurance on the lives of members of senior management. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel.

Additionally, our ability to effectively recruit and retain qualified officers and directors could also be adversely affected if we experience difficulty in obtaining adequate directors’ and officers’ liability insurance. We may be unable to maintain sufficient insurance as a public company to cover liability claims made against our officers and directors. If we are unable to adequately insure our officers and directors, we may not be able to retain or recruit qualified officers and directors to manage the Company.

Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal control requirements for publicly traded companies.

As a public company, we will operate in an increasingly challenging regulatory environment which requires us to comply with the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the related rules and regulations of the SEC and securities exchanges, expanded disclosures, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. However, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, until the date we are no longer an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, because we are taking advantage of the exemptions contained in the JOBS Act. We will remain an emerging growth company until, subject to certain conditions, the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our ordinary shares that is held by non-affiliates exceeds $700.0 million as of the prior June 30, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

To date, our independent public accountant has never conducted a review of our internal control for the purpose of providing the reports required by these rules. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall.

To build our finance infrastructure, we will need to improve our accounting systems, disclosure policies, procedures and controls. If we are unsuccessful in building an appropriate accounting infrastructure, we may not be able to prepare and disclose, in a timely manner, our financial statements and other required disclosures, or comply with existing or new reporting requirements. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Capital Market or other adverse consequences that would materially harm our business. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

We may experience rapid and substantial growth in order to achieve our operating plans, which will place a strain on our human and capital resources. Successful implementation of our business plan will require management of growth, which will result in an increase in the level of responsibility for management personnel. We currently have a minimum number of employees and in order to continue the clinical development of our products, we will need to substantially increase our operations, including expanding our employee base of managerial, operational and financial personnel. We currently intend to establish additional infrastructure in the United States and Europe, and therefore we may require additional funds. Any future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. To that end, we must be able to, among other things:

- manage our clinical trials and the regulatory process effectively;
- develop our administrative, accounting and management information systems and controls;
- hire and train additional qualified personnel; and
- integrate current and additional management, administrative, financial and sales and marketing personnel.

If we are unable to establish, scale-up and implement improvements to our control systems in an efficient or timely manner, or if we encounter deficiencies in existing systems and controls, investors may choose not to invest in us, which could cause our share price to decline and negatively impact our ability to successfully commercialize our product candidate and future product candidates.

Failure to attract and retain sufficient numbers of talented employees will further strain our human resources and could impede our growth or result in ineffective growth. If we are unable to manage our growth effectively, our losses could materially increase and it will have a material adverse effect on our business, results of operations and financial condition.

Our business, including our ability to raise capital, may be affected by macroeconomic conditions.

A deterioration in global economic conditions and uncertainties may have an adverse effect on our business. For instance, interest rates, the liquidity of the credit markets and the volatility of the capital markets could also affect the value of our investments, if any, and our ability to liquidate such investments in order to fund our operations. Interest rates and the ability to access credit markets could also adversely affect the ability of patients and distributors to purchase, pay for and effectively distribute our products.

Moreover, in past years, the U.S. and global economies have taken a downturn as the result of the deterioration in the credit markets and related financial crisis as well as a variety of other factors including, among other things, extreme volatility in security prices, diminished liquidity and credit availability, ratings downgrades of certain investments and declining valuations of others, global supply and demand of various commodities, such as gas and oil and pricing of thereof, as well as geopolitical risks, including that related to China. The U.S. and certain foreign governments have recently taken actions in an attempt to address and rectify these extreme market and economic conditions by providing liquidity and stability to the financial markets. If the actions taken by these governments are not successful, the continued economic decline may cause a significant impact on our ability to raise capital, if needed, on a timely basis and on acceptable terms or at all. In addition, we rely and intend to rely on third-parties, including our clinical research organizations, third-party manufacturers and second source suppliers, and certain other important vendors and consultants. As a result of the current volatile and unpredictable global economic situation, there may be a disruption or delay in the performance of our third-party contractors and suppliers. If such third-parties are unable to satisfy their contractual commitments to us, our business could be severely adversely affected.

The Israeli Ministry of Health will not permit us to conduct multiple biopsies as contemplated in our ARREST Study of Aramchol in Israel.

On March 9, 2015, we announced that we had begun the enrollment stage of our Phase IIB ARREST Study of Aramchol in 240 biopsy-diagnosed OD patients with NASH. The primary endpoint of the study is a significant reduction of liver fat, as measured by magnetic resonance spectroscopy, or MRS, which is a noninvasive and sensitive method for quantification of the amount of fat in the liver. The main secondary endpoint of the ARREST Study is resolution of NASH on biopsies, which can be assessed only at the completion of the study and by repeated liver biopsies. We are conducting a portion of our ARREST Study in Israel. While, the Israeli Ministry of Health has granted us approval to conduct our ARREST Study including patients that underwent a liver biopsy independently and previously to the study (as warranted by their medical condition), it has taken exception to the necessity of conducting a second biopsy at the end of the trial period, as specified by the trial protocol. As this position is inconsistent with the already established guidance by the FDA and the EMA, it was unexpected. We are not expecting that the Israeli Ministry of Health will reverse its preliminary position, and as such, we reconfigured our recruitment targets in Israel to include patients who have undergone liver biopsies no more than six months prior to enrolling in the ARREST Study. After conducting a close dialogue with the Israeli Ministry of Health, we did not succeed in changing their position concerning the second biopsy, and patients who will not undergo a second biopsy as part of the ARREST Study will be considered treatment failure. However we can perform a statistical analysis for the sub group that underwent the second biopsy and based on the results of such group (even trends of improvement) continue to a pivotal phase III study.

Contemporaneously, we also announced on March 9, 2015 that we had expanded our clinical activities to include patient recruitment for the ARREST Study in the United States. Professor Vlad Ratziu, from the University Pierre et Marie Curie in Paris, an internationally acclaimed key opinion leader, is the ARREST Study's global principal investigator, and Professor Rohit Loomba, from the University of California San Diego School of Medicine, is the ARREST Study's U.S.-based principal investigator. We expanded our patient recruitment into the United States because we believe that expanding our clinical activities into the United States will improve the ARREST Study's breadth and relevance, including potentially allowing us to immediately commence Phase III clinical trials in NASH in OD patients in the United States without any additional clinical requirements.

Additional clinical trials may divert a significant amount of Company resources and may ultimately be unsuccessful.

During 2016, we intend to expand our clinical operations for Aramchol to multiple other indications in order to expand our pipeline, commercial potential and ultimately de-risk the Company for the success of any one given trial. However, such activities will require significant time, funds and Company resources. There can be no assurance that these studies will be successful.

Risks Related to Our Reliance on Third Parties

We have no manufacturing capacity and anticipate reliance on third-party manufacturers for our products.

We do not currently operate manufacturing facilities for the production of Aramchol or its API. We still have not, and may never, develop facilities for the manufacture of product candidates or products for clinical trials or commercial purposes. We rely, and for the foreseeable future, will continue to rely, on third-party manufacturers to produce bulk drug products required for our clinical trials. We plan to initially rely upon contract manufacturers and, potentially, collaboration partners, to manufacture commercial quantities of our product candidates, if and when approved for marketing by the applicable regulatory authorities. Our contract manufacturers have not completed process validation for Aramchol or the Aramchol API manufacturing processes. If our contract manufacturers and their facilities, as applicable, are not approved by the FDA, or other applicable regulatory authorities, our commercial supply of the drug substance will be significantly delayed and may result in significant additional costs. We purchase finished Aramchol from a third-party under a clinical supply agreement. If we need to identify an additional finished product manufacturer, we would not be able to do so without significant delay and likely significant additional cost.

A failure by our contract manufacturer to achieve and maintain high manufacturing standards, in accordance with applicable good manufacturing practices (GMPs) and other applicable regulatory requirements could result in patient injury or death, product shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost

overruns or other problems that could seriously harm our business. Contract manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel.

Our existing manufacturers and any future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business. In the event of a natural disaster, business failure, strike or other difficulty, we may be unable to replace a third-party manufacturer in a timely manner and the production of Aramchol would be interrupted, resulting in delays and additional costs.

We intend to rely primarily on third parties to market and sell Aramchol.

We have no sales or distribution capabilities. To the extent we rely on third parties to commercialize Aramchol, if marketing approval is obtained, we may receive less revenue than if we commercialize Aramchol ourselves. In addition, we would have less control over the sales efforts of any third parties involved in our commercialization efforts. In the event we are unable to collaborate with a third-party marketing and sales organization to commercialize Aramchol, particularly for broader patient populations, our ability to generate revenue will be limited.

Although we may ultimately develop a marketing and sales force with technical expertise and supporting distribution capabilities in the longer term, we do not currently intend to do so and, as such, we will be unable to market our product candidate directly in the near future. To promote any of our potential products through third parties, we will have to locate acceptable third parties for these functions and enter into agreements with them on acceptable terms, and we may not be able to do so. Any third-party arrangements we are able to enter into may result in lower revenues than we could achieve by directly marketing and selling our potential products. In addition, to the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, as well as the terms of our agreements with such third parties, which cannot be predicted in most cases at this time. As a result, we might not be able to market and sell our products in the United States or overseas, which would have a material adverse effect on us.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our current and potential future product candidates.

We intend to seek collaboration arrangements with pharmaceutical or biotechnology companies for the development and commercialization of our current and potential future product candidates. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision making authority. Moreover, collaborations with pharmaceutical or biotechnology companies and other third parties are often terminated or allowed to expire by the other party. Any lack of effort or ability by our collaborators or any such disagreement, termination or expiration could adversely affect us financially and could harm our business reputation.

We depend on third parties to conduct our clinical trials.

We rely on third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories to oversee most of the operations of our clinical trials and to perform data collection and analysis. As a result, we may face additional delays outside of our control if these parties do not perform their obligations in a timely fashion or in accordance with regulatory requirements. If these third parties do not successfully carry out their

contractual duties or obligations and meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or for other reasons, our financial results and the commercial prospects for Aramchol or any other potential product candidates could be harmed, our costs could increase and our ability to obtain regulatory approval and commence product sales could be delayed.

Risks Related to Our Intellectual Property

The failure to obtain or maintain patents, licensing agreements and other intellectual property rights that are sufficiently broad and protective could impact our ability to compete effectively.

To compete effectively, we must develop and maintain a proprietary position with regard to our own technologies, intellectual property, licensing agreements, product candidates and business. Legal standards relating to the validity and scope of claims in the biotechnology and biopharmaceutical fields are still evolving. We cannot predict the scope and extent of patent protection for Aramchol because the patent positions of pharmaceutical products are complex and uncertain. Therefore, the degree of future protection for our proprietary rights in our core technologies and any product candidates or products that might be developed using these technologies is also uncertain. The risks and uncertainties that we face with respect to our patents and other proprietary rights include, but are not limited to, the following:

- while the patents we own have been issued, pending patent applications we have filed may not result in issued patents or may take longer than we expect to result in issued patents;
- we may be subject to interference or reexamination proceedings in the U.S.;
- we may be subject to opposition proceedings in certain foreign countries;
- any patents that are issued may not provide meaningful protection for any significant period of time, if at all;
- any issued patents may not be broad or strong enough to prevent competition from other products including identical or similar products;
- we may not be able to develop additional proprietary technologies that are patentable;
- there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim;
- there may be other patents or pending patent applications existing in the patent landscape that will affect our freedom to operate for Aramchol;
- other companies may challenge and invalidate patents licensed or issued to us or our customers;
- a court could determine that a competitor's technology or product does not infringe our patents;
- other companies may independently develop similar or alternative technologies, or duplicate our technologies;
- other companies may design around technologies we have licensed or developed;
- if we are not awarded patents or if issued patents expire or are declared invalid or not infringed, there may be no protections against competitors making generic equivalents;
- enforcement of patents is complex, uncertain and expensive, and our patents may be found invalid or enforceable;
- our patents could irretrievably lapse due to failure to pay fees or otherwise comply with regulations, or could be subject to compulsory licensing; and

- if we encounter delays in our development or clinical trials, the period of time during which we could market our products under patent protection would be reduced.

We cannot be certain that patents will be issued as a result of any of our pending applications, and we cannot be certain that any of our issued patents, whether issued pursuant to our pending applications or licensed from third parties, will give us adequate protection from competing products. For example, issued patents may be circumvented or challenged, declared invalid or unenforceable, or narrowed in scope. In addition, because publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first to make our inventions or to file patent applications covering those inventions. If any of our composition of matter patents, or pending applications, was subject to a successful challenge or failed to issue, our business and competitive advantage could be significantly affected. Our current patents will expire or they may otherwise cease to provide meaningful competitive advantage, and we may be unable to adequately develop new technologies and obtain future patent protection to preserve our competitive advantage or avoid adverse effects on our business.

The composition of matter patents pertaining to Aramchol will expire on March 25, 2019 worldwide outside of Israel and on April 8, 2018 in Israel. We do not expect that we will be able to submit an NDA seeking approval of Aramchol prior to the composition of matter patents' expiration date. However, because Aramchol may be a new chemical entity, or NCE, following approval of an NDA, if we are the first applicant to obtain NDA approval, we may be entitled to five years of data and market exclusivity in the United States with respect to such NCE**.** Analogous data and market exclusivity provisions, of varying duration, may be available in Europe and other foreign jurisdictions. The Company also has rights under its pharmaceutical use issued patents with respect to Aramchol, which provide patent exclusivity within the Company's field of activity until the last of such patents expires in 2030. While the Company believes that it may be able to protect its exclusivity in its field of activity through such use patent portfolio and such period of exclusivity, the lack of composition of matter patent protection may diminish the Company's ability to maintain a proprietary position for its intended uses of Aramchol. Moreover, the Company cannot be certain that it will be the first applicant to obtain an FDA approval for any indication of Aramchol and it cannot be certain that it will be entitled to NCE exclusivity. Such diminution of Aramchol's proprietary position could have a material adverse effect on our business, results of operation and financial condition.

Others may obtain issued patents that could prevent us from commercializing our product candidates or require us to obtain licenses requiring the payment of significant fees or royalties in order to enable us to conduct our business. As to those patents that we have licensed, our rights depend on maintaining our obligations to the licensor under the applicable license agreement, and we may be unable to do so.

In addition to patents and patent applications, we depend upon trade secrets and proprietary know-how to protect our proprietary technology. We require our employees, consultants, advisors and collaborators to enter into confidentiality agreements that prohibit the disclosure of confidential information to any other parties. We also require our employees and consultants to disclose and assign to us their ideas, developments, discoveries and inventions. These agreements may not, however, provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure.

Our potential development of Aramchol salts may not result in improved bioavailability compared to the existing form of Aramchol. Furthermore, although we have submitted patent applications for our Aramchol salts in development, there is no assurance that we will receive any patents for them, and even if we receive one or more patents for our Aramchol salts in development, they may be of little or no commercial value.

As part of our ongoing pre-formulation studies, we have confirmed that several Aramchol salts have improved solubility and intestinal permeability as compared to the existing form of Aramchol. We have recently submitted new patent applications to protect such salts. In addition, we intend to plan and conduct further formulation development in order to test the possibility of using Aramchol salts in future clinical studies. If we decide to develop the formulations of Aramchol salts due to the improvement in solubility and bioavailability and longer patent protection, we may conduct an appropriate bioequivalence study, or studies of the biological equivalence of two proprietary preparations of a drug, prior to administering an Aramchol salt formulation to patients in our clinical studies.

If we commence animal PK studies and formulation development in order to test the bioavailability of the Aramchol salt compounds, the results might not support the claims sought by us. Success in our earlier pre-formulation studies does not ensure that later studies will be successful, and the results of later studies may not replicate the results of our prior pre-formation studies. Furthermore, either or both of the animal PK and formulation development studies may fail to demonstrate that the Aramchol salts result in an improvement in solubility and bioavailability. Any such failure may cause us to abandon the Aramchol salt compounds and may delay development of other product candidates. If the animal PK studies do not support our claims, the completion of development of such potential product candidates may be significantly delayed or abandoned, which will significantly impair our ability to generate revenues and will materially adversely affect our results of operations.

There can be no assurance that the U.S. Patent and Trademark Office, or the USPTO, will issue any patents based on the patent applications that we submitted to protect our Aramchol salts, nor, should the USPTO issue any patents to us with respect to the Aramchol salts, that we will be provided with adequate protection against potentially competitive products. Furthermore, if the USPTO issues us one or more patents for the Aramchol salts, there can be no assurance that the issued patents will be of any commercial value, or that private parties or competitors will not successfully challenge these patents or circumvent these patents in the United States or abroad. In the absence of adequate patent protection, our business may be adversely affected by competitors who develop comparable technology or products.

We may not be able to enforce our intellectual property rights throughout the world. This risk is exacerbated for us because we expect Aramchol will be manufactured and used in a number of foreign countries.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. This risk is exacerbated for us because we expect Aramchol will be manufactured and used in a number of foreign countries.

The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our other intellectual property rights. For example, several foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Although most jurisdictions in which the Company has applied for, intends to apply for, or has been issued patents have patent protection laws similar to those of the United States, some of them do not. For example, the Company expects to do business in South America, Eurasia, China and Indochina in the future and the countries in these regions may not provide the same or similar protection as that provided in the United States. Additionally, due to uncertainty in patent protection law, the Company has not filed applications in many countries where significant markets exist, including South American countries, Eurasian countries, African countries and Taiwan.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property.

We may be unable to protect the intellectual property rights of the third parties from whom we may license certain of our intellectual property or with whom we have entered into other strategic relationships, which could have a material adverse effect on our business, results of operations and financial condition.

Certain of our intellectual property rights may be licensed from third parties, including universities and/or strategic partners. Such third parties may determine not to or fail to protect the intellectual property rights that we license from them and we may be unable to defend such intellectual property rights on our own or we may have to undertake costly litigation to defend the intellectual property rights of such third parties. There can be no assurances that we will

continue to have proprietary rights to any of the intellectual property that we license from such third parties or otherwise have the right to use through similar strategic relationships. Any loss or limitations on use with respect to such intellectual property licensed from third parties or otherwise obtained from third parties with whom we have entered into strategic relationships could have a material adverse effect on our business, results of operations and financial condition.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing, or increase the costs of commercializing, our products.

Our commercial success depends significantly on our ability to operate without infringing the patents and other intellectual property rights of third parties. For example, there could be issued patents of which we are not aware that our products infringe. There also could be patents that we believe we do not infringe, but that we may ultimately be found to infringe. Moreover, patent applications are in some cases maintained in secrecy until patents are issued. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and patent applications were filed. Because patents can take many years to issue, there may be currently pending applications of which we are unaware that may later result in issued patents that our products infringe. For example, pending applications may exist that provide support or can be amended to provide support for a claim that results in an issued patent that our product infringes.

Third parties may assert that we are employing their proprietary technology without authorization. If a court held that any third-party patents are valid, enforceable and cover our products or their use, the holders of any of these patents may be able to block our ability to commercialize our product candidates or products unless we obtained a license under the applicable patents, or until the patents expire. In addition to litigation proceedings which may be filed against us, we may not be able to enter into licensing arrangements or make other arrangements at a reasonable cost or on reasonable terms. Any inability to secure licenses or alternative technology could result in delays in the introduction of our products or lead to prohibition of the manufacture or sale of products by us.

We may be unable to adequately prevent disclosure and unauthorized use of trade secrets and other proprietary information by third parties.

Our ability to obtain and maintain patent protection and trade secret protection for our intellectual property and proprietary technologies, our products and their uses is important to our commercial success. We rely on a combination of patent, copyright, trademark and trade secret laws, non-disclosure and confidentiality agreements, licenses, assignment of inventions agreements and other restrictions on disclosure and use to protect our intellectual property rights.

We also rely on trade secrets to protect our proprietary know-how and technological advances, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. Failure to obtain or maintain trade secret protection could enable competitors to use our proprietary information to develop products that compete with our product candidates or products or cause additional material adverse effects upon our competitive business position.

We cannot be certain that the steps that we have taken will prevent the misappropriation or other violation of our confidential information and other intellectual property, particularly in foreign countries in which laws may not protect our proprietary rights as fully as in the United States and other developed economies. Moreover, if we lose any key personnel, we may not be able to prevent the unauthorized disclosure or use of our technical knowledge or other trade secrets by those former employees. If we are unable to maintain the security of our proprietary technology, this could materially adversely affect our competitive advantage, business and results of operations.

Under applicable U.S. and Israeli law, we may not be able to enforce covenants not to compete and therefore may be unable to prevent our competitors from benefiting from the expertise of some of our former employees. In addition, employees may be entitled to seek compensation for their inventions irrespective of their agreements with

us, which in turn could impact our future profitability.

We generally enter into non-competition agreements with our employees and certain key consultants, or our employment and consulting agreements contain non-competition provisions. These agreements, to the extent they are in place and in effect, prohibit our employees and certain key consultants, if they cease working for us, from competing directly with us or working for our competitors or clients for a limited period of time. We may be unable to enforce these agreements under the laws of the jurisdictions in which our employees work and it may be difficult for us to restrict our competitors from benefitting from the expertise our former employees or consultants developed while working for us. For example, Israeli courts have required employers seeking to enforce non-compete undertakings of a former employee to demonstrate that the competitive activities of the former employee will harm one of a limited number of material interests of the employer which have been recognized by the courts, such as the secrecy of a company's confidential commercial information or the protection of its intellectual property. If we cannot demonstrate that such interests will be harmed, we may be unable to prevent our competitors from benefiting from the expertise of our former employees or consultants and our ability to remain competitive may be diminished.

In addition, Chapter 8 to the Israeli Patents Law, 5727-1967, or the Patents Law, deals with inventions made in the course of an employee's service and during his or her term of employment, whether or not the invention is patentable, or service inventions. Section 134 of the Patents Law provides that if there is no agreement that explicitly determines whether the employee is entitled to compensation for the service inventions and the extent and terms of such compensation, such determination will be made by the Compensation and Rewards Committee, a statutory committee of the Israeli Patents Office. Although our employees have agreed to assign to us service invention rights, we may face claims demanding remuneration in consideration for assigned inventions. Decisions by the Compensation and Rewards Committee and Israeli courts have created some uncertainty in this area, as some decision have held that employees may be entitled to remuneration for their service inventions despite having specifically waived any such rights. 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.

Any lawsuits relating to infringement of intellectual property rights necessary to defend ourselves or enforce our rights will be costly and time consuming.

We may be required to initiate litigation to enforce our rights or defend our activities in response to alleged infringement of a third-party. In addition, we may be sued by others who hold intellectual property rights and who claim that their rights are infringed by Aramchol or any of our future products or product candidates. These lawsuits can be very time consuming and costly. There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally.

A third-party may claim that we are using inventions claimed by their patents and may go to court to stop us from engaging in our normal operations and activities, such as research, development and the sale of any future products. Such lawsuits are expensive and would consume time and other resources. There is a risk that such court will decide that we are infringing the third-party's patents and will order us to stop the activities claimed by the patents, redesign our products or processes to avoid infringement or obtain licenses, which may not be available on commercially reasonable terms. In addition, there is a risk that a court will order us to pay the other party damages for infringement.

Moreover, there is no guarantee that any prevailing patent owner would offer us a license so that we could continue to engage in activities claimed by the patent, or that such a license, if made available to us, could be acquired on commercially acceptable terms. In addition, third parties may, in the future, assert other intellectual property infringement claims against us with respect to our product candidates, technologies or other matters.

In addition, our patents and patent applications could face other challenges, such as interference proceedings, opposition proceedings and re-examination proceedings. Any of these challenges, if successful, could result in the invalidation of, or in a narrowing of the scope of, any of our patents and patent applications subject to challenge. Any of these challenges, regardless of their success, would likely be time consuming and expensive to defend and resolve and would divert our management's time and attention.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity. Therefore, obtaining and enforcing pharmaceutical patents is costly, time-consuming and inherently uncertain. In particular, the United States has recently enacted, and is currently implementing, wide-ranging patent reform legislation. The United States Supreme Court has ruled on several patent cases in recent years, and could do so again in the future, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by applicable courts and legislatures in the countries in which we may pursue patent protection, including those of the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents and the interpretations of such laws could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

Risks Related to Ownership of Our Ordinary Shares

The market price of our ordinary shares is volatile and you may sustain a complete loss of your investment.

Since our initial public offering, the trading price of our ordinary shares has been volatile and is likely to continue to be volatile. In addition, the trading volume is and has been volatile and oftentimes relatively illiquid. The following factors, some of which are beyond our control, in addition to other risk factors described in this section, may have a significant impact on the market price and trading volume of our ordinary shares:

- delays in existing clinical trials due to an inability to enroll patients at the expected pace, among other factors;
- inability to obtain the approvals necessary to commence further clinical trials;
- unsatisfactory or inconclusive results of clinical trials;
- termination of clinical trials;
- adverse events in our ongoing clinical trials;
- announcements of regulatory approval or the failure to obtain it, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;

- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to Aramchol;
- any adverse changes to our relationship with manufacturers or suppliers;
- any product liability actions or intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability or our failure to meet expectations;
- our commencement of, or involvement in, litigation;
- any major changes in our board of directors, or our Board, management or other key personnel;
- legislation in the United States, Europe and other foreign countries relating to the sale or pricing of pharmaceuticals;

- announcements by us of significant strategic partnerships, out-licensing, in-licensing, joint ventures, acquisitions or capital commitments;
- expiration or terminations of licenses, research contracts or other collaboration agreements;
- public concern as to the safety of drugs we, our licensees or others develop;
- success of research and development projects;
- variations in our and our competitors' results of operations;
- changes in earnings estimates, cashflow guidance, or recommendations by securities analysts;
- developments by our licensees, if any; and
- future issuances of ordinary shares or other securities.

These factors and any corresponding price fluctuations may materially and adversely affect the market price and trading volume of our ordinary shares and result in substantial losses by our investors.

In addition, the stock market in general, and the Nasdaq Capital Market and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of our Company and that of small companies. Broad market and industry factors may negatively affect the market price of our ordinary shares, regardless of our actual operating performance. Further, a systemic decline in the financial markets and related factors beyond our control may cause our share price to decline rapidly and unexpectedly. Price volatility of our ordinary shares might be worse if the trading volume of our ordinary shares is low. Following periods of market volatility, shareholders may institute securities class action litigation. If we were involved in securities litigation, it could have a substantial cost and divert resources and attention of management from our business, even if we are successful. Future sales of our ordinary shares could also reduce the market price of such stock. Any adverse determination in litigation could also subject us to significant liabilities.

Moreover, the liquidity of our ordinary shares is limited, not only in terms of the number of shares that can be bought and sold at a given price, but by delays in the timing of transactions and reduction in security analysts' and the media's coverage of us, if any. These factors may result in lower prices for our ordinary shares than might otherwise be obtained and could also result in a larger spread between the bid and ask prices for our ordinary shares. In addition,

without a large float, our ordinary shares are less liquid than the stock of companies with broader public ownership and, as a result, the trading prices of our ordinary shares are more volatile. In the absence of an active public trading market, an investor may be unable to liquidate its investment in our ordinary shares. Trading of a relatively small volume of our ordinary shares may have a greater impact on the trading price of our stock than would be the case if our public float were larger. We cannot predict the prices at which our ordinary shares will trade in the future.

Our principal shareholders, President and Chief Executive Officer and directors currently own approximately 42% and 40% of our outstanding ordinary shares on a diluted basis and non-diluted basis, respectively. They will therefore be able to exert significant control over matters submitted to our shareholders for approval.

Our President and Chief Executive Officer, directors and shareholders that own more than 5% of our outstanding ordinary shares own approximately 412 and 40% of our ordinary shares on a fully diluted basis and non-diluted basis, respectively. As a result, these shareholders, if they acted together, could significantly influence or even unilaterally approve matters requiring approval by our shareholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of these shareholders may not always coincide with our interests or the interests of other shareholders. This significant concentration of share ownership may adversely affect the trading price for our ordinary shares because investors often perceive disadvantages in owning stock in companies with controlling shareholders.

Sales of a substantial number of our ordinary shares in the public market by our existing shareholders could cause our share price to fall.

Sales of a substantial number of our ordinary shares in the public market, or the perception that these sales might occur, could depress the market price of our ordinary shares and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our ordinary shares. Prior to the consummation of our initial public offering and in accordance with the terms of the Tax Pre-Ruling, the holders of substantially all of our then-outstanding approximately seven million ordinary shares and options agreed not to sell or dispose of our ordinary shares for a period of two years following the consummation of the Reorganization, subject to certain exceptions. To date, the lock-up period has expired and all of our outstanding shares are eligible for unrestricted sale. In addition, shares issued or issuable upon exercise of options and warrants vested as of the expiration of the lock-up period are eligible for sale as of February 4, 2016. Sales of shares by these shareholders would likely result in the supply of our ordinary shares far exceeding the demand for our ordinary shares and could have a material adverse effect on the trading price of our ordinary shares.

Raising additional capital would cause dilution to our existing shareholders, and may restrict our operations or require us to relinquish rights.

We may seek additional capital through a combination of private and public equity offerings, at-the-market issuances, equity-linked and structured transactions, debt (straight, convertible, or otherwise) financings, collaborations and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic alliance and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates, or grant licenses on terms that are not favorable to us.

In anticipation of the same, we registered $150 million of our ordinary shares on July 2, 2015, pursuant to a registration statement on Form F-3, which was declared effective by the SEC. Depending upon market liquidity at the time, a sale of shares registered pursuant to such registration statement at any given time could cause the trading price of our common stock to decline.

Our U.S. shareholders may suffer adverse tax consequences due to our classification as a passive foreign investment company, or PFIC.

Generally, if for any taxable year 75% or more of our gross income is passive income, or at least 50% of our assets are held for the production of, or produce, passive income, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. Based upon our review of our financial data, we have determined that we are currently a PFIC, and we likely will continue to be a PFIC, at least until we develop a source of significant operating revenues. If we were to be characterized as a PFIC for U.S. federal income tax purposes in any taxable year during which a U.S. Holder, as defined in "Item 10. Additional Information—E. Taxation— Certain U.S. Federal Income Tax Considerations," owns ordinary shares, such U.S. Holder could face adverse U.S. federal income tax consequences. For example, such U.S. Holder could be liable to additional taxes and interest charges upon certain distributions by us and any gain recognized on a sale, exchange or other disposition of our shares, whether or not we continue to be characterized as a PFIC. One way in which certain of the adverse consequences of PFIC status can be mitigated is for a U.S. Holder to make an election to treat us as a qualified electing fund, or QEF. A shareholder making the QEF election is required for each taxable year to include in income a pro rata share of the ordinary earnings and net capital gain of the QEF, subject to a separate election to defer payment of taxes, which deferral is subject to an interest charge. An election to treat us as a QEF will not be available if we do not provide the information necessary to make such an election. It is not expected that a U.S. Holder will be able to make a QEF election because we do not intend to provide U.S. Holders with the information necessary to make a QEF election. See also "Item 10. Additional Information—E. Taxation— Certain U.S. Federal Income Tax Considerations."

If we are unable to satisfy the requirements of Section 404 as they apply to a foreign private issuer and emerging growth company, or our internal controls over financial reporting are not effective, the reliability of our financial statements may be questioned and our share price may suffer.

We became subject to the requirements of the Sarbanes-Oxley Act when our ordinary shares were listed on the Nasdaq Capital Market. Section 404 requires companies subject to the reporting requirements of the U.S. securities laws to do a comprehensive evaluation of its and its subsidiaries' internal controls over financial reporting. To comply with this statute, we will be required to document and test our internal control procedures and our management will be required to assess and issue a report concerning our internal controls over financial reporting. Pursuant to the JOBS Act, we will be classified as an "emerging growth company." Under the JOBS Act, emerging growth companies are exempt from certain reporting requirements, including the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act. Under this exemption, our auditor will not be required to attest to and report on management's assessment of our internal controls over financial reporting during a five year transition period. We will need to prepare for compliance with Section 404 by strengthening, assessing and testing our system of internal controls to provide the basis for our report. However, the continuous process of strengthening our internal controls and complying with Section 404 is complicated and time-consuming. Furthermore, as our business continues to grow both domestically and internationally, our internal controls will become more complex and will require significantly more resources and attention to ensure our internal controls remain effective overall. During the course of its testing, our management may identify material weaknesses or significant deficiencies, which may not be remedied in a timely manner to meet the deadline imposed by the Sarbanes-Oxley Act. If our management cannot favorably assess the effectiveness of our internal controls over financial reporting, or our independent registered public accounting firm identifies material weaknesses in our internal controls, investor confidence in our financial results may weaken, and the market price of our securities may suffer. Nevertheless, as a foreign private issuer that is an emerging growth company, we are not be required to comply with the auditor attestation requirements of Section 404 for up to five fiscal years after the date of our initial public offering. See "Item 5. Operating and Financial Review and Prospects—Jumpstart Our Business Startups Act of 2012" for more detail regarding our status as an emerging growth company.

If the securities analysts that current cover our stock, or will do so in the future, or industry analysts do not publish or cease publishing research or reports about us, our business or our market, or if they adversely change their recommendations or publish negative reports regarding our business or our shares, our share price and trading volume could be negatively impacted.

The trading market for our ordinary shares is influenced by the research and reports that industry or securities analysts may publish about us, our business, our market or our competitors. We do not have any control over these analysts and we cannot provide any assurance that analysts will cover us or provide favorable coverage. If any of the analysts who do cover, or may cover us in the future, adversely change their recommendation regarding our shares, or provide more favorable relative recommendations about our competitors, our share price would likely decline. If any analyst who cover us to cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could negatively impact our share price or trading volume.

Because we do not intend to declare cash dividends on our ordinary shares in the foreseeable future, shareholders must rely on appreciation of the value of our ordinary shares for any return on their investment.

We have never declared or paid cash dividends on our ordinary shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Moreover, the Israeli Companies Law, 5759-1999, as amended, or the Companies Law, imposes certain restrictions on our ability to declare and pay dividends. See “Item 8. Financial Information—Consolidated Financial Statements and Other Financial Information—Dividend Policy” for additional information.

The requirements associated with being a public company require significant company resources and management attention.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, or the Exchange Act, the Sarbanes-Oxley Act, the listing requirements of the Nasdaq Capital Market, on which our ordinary shares are traded, and other applicable securities rules and regulations. The Exchange Act requires that we file periodic reports with respect to our business and financial condition and maintain effective disclosure controls and procedures and internal control over financial reporting. In addition, subsequent rules implemented by the SEC and the Nasdaq Capital Market may also impose various additional requirements on public companies. As a result, we incurred and will continue to incur additional legal, accounting and other expenses that we did not incur as a privately-held company, particularly after we are no longer an "emerging growth company" as defined in the JOBS Act. Further, the need to establish the corporate infrastructure demanded of a public company may divert management's attention from implementing our development plans. We have made and will continue to make changes to our corporate governance standards, compensation policy, disclosure controls and financial reporting and accounting systems to meet our reporting obligations and applicable law. The measures we take, however, may not be sufficient to satisfy our obligations as a public company, which could subject us to delisting of our ordinary shares, fines, sanctions and other regulatory action and potentially civil litigation.

The JOBS Act will allow us to postpone the date by which we must comply with some of the laws and regulations intended to protect investors and to reduce the amount of information we provide in our reports filed with the SEC, which could undermine investor confidence in our company and adversely affect the market price of our ordinary shares.

For so long as we remain an "emerging growth company" as defined in the JOBS Act, we intend to take advantage of certain exemptions from various requirements that are applicable to public companies that are not "emerging growth companies" including:

- the provisions of the Sarbanes-Oxley Act requiring that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting;

- the "say on pay" provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, or the Dodd-Frank Act, requiring a non-binding shareholder vote to approve compensation of certain executive officers, and the Dodd-Frank Act's "say on golden parachute" provisions requiring a non-binding shareholder vote to approve golden parachute arrangements for certain executive officers in connection with mergers and certain other business combinations and some of the disclosure requirements of the Dodd-Frank Act relating to compensation of our President and Chief Executive Officer;

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- any rules that may be adopted by the Public Company Accounting Oversight Board, or the PCAOB, requiring mandatory audit firm rotation or a supplement to the auditor's report on the financial statements; and

- our ability to furnish two rather than three years of income statements and statements of cash flows in various required filings.

We cannot predict if investors will find our ordinary shares less attractive because we may rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares, and our share price may become more volatile and decline.

As a "foreign private issuer," we are permitted to and currently do follow certain home country corporate governance practices instead of otherwise applicable SEC and Nasdaq Capital Market requirements, which may result in less protection than is accorded to investors under rules applicable to domestic U.S. issuers.

As a "foreign private issuer," we are permitted to, and currently do, follow certain home country corporate governance practices instead of those otherwise required under the Listing Rules of the Nasdaq Capital Market for domestic U.S. issuers. For instance, we currently follow home country practice in Israel with regard to, among other things, director nomination procedures, quorum requirements and approval of compensation of officers. In addition, we may follow our home country law instead of the Listing Rules of the Nasdaq Capital Market that require that we obtain shareholder approval for certain dilutive events, such as the establishment or amendment of certain equity based compensation plans, an issuance that will result in a change of control of the company, certain transactions other than a public offering involving issuances of a 20% or greater interest in the company, and certain acquisitions of the stock or assets of another company. Following our home country governance practices as opposed to the requirements that would otherwise apply to a U.S. company listed on the Nasdaq Capital Market may provide less protection to you than what is accorded to investors under the Listing Rules of the Nasdaq Capital Market applicable to domestic U.S. issuers. See "Item 16G. Corporate Governance."

In addition, as a "foreign private issuer," we are exempt from the rules and regulations under the Exchange Act related to the furnishing and content of proxy statements and certain individual executive compensation information, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. Furthermore, as a "foreign private issuer," we are also not subject to the requirements of Regulation FD (Fair Disclosure) promulgated under the Exchange Act. These exemptions and leniencies reduce the frequency and scope of information and protections to which you are entitled as an investor.

Because our ordinary shares may be a "penny stock," it may be more difficult for investors to sell their ordinary shares, and the market price of our ordinary shares may be adversely affected.

Our ordinary shares may be a "penny stock" if, among other things, the stock price is below $5.00 per share, it is not listed on a national securities exchange or we have not met certain net tangible asset or average revenue requirements. Broker-dealers who sell penny stocks must provide purchasers of these stocks with a standardized risk-disclosure document prepared by the SEC. This document provides information about penny stocks and the nature and level of risks involved in investing in the penny-stock market. A broker must also give a purchaser, orally or in writing, bid and offer quotations and information regarding broker and salesperson compensation, make a written determination that the penny stock is a suitable investment for the purchaser, and obtain the purchaser's written agreement to the purchase. Broker-dealers must also provide customers that hold penny stock in their accounts with such broker-dealer a monthly statement containing price and market information relating to the penny stock. If a penny stock is sold to an investor in violation of the penny stock rules, the investor may be able to cancel its purchase and get its money back.

If applicable, the penny stock rules may make it difficult for investors to sell their ordinary shares. Because of the rules and restrictions applicable to a penny stock, there is less trading in penny stocks and the market price of our ordinary shares may be adversely affected. Also, many brokers choose not to participate in penny stock transactions. Accordingly, investors may not always be able to resell their ordinary shares publicly at times and prices that they feel are appropriate and the market price of our ordinary shares may be adversely affected.

Our ordinary shares are listed on the Nasdaq Capital Market. As such, we must meet the Nasdaq Capital Market's continued listing requirements and other Nasdaq rules, or we may risk delisting. Delisting could negatively affect the price of our ordinary shares, which could make it more difficult for us to sell securities in a financing and for you to sell your ordinary shares.

Our ordinary shares are listed on the Nasdaq Capital Market. As such, we are required to meet the continued listing requirements of the Nasdaq Capital Market and other Nasdaq rules, including those regarding director independence and independent committee requirements, minimum stockholders' equity, minimum share price and certain other corporate governance requirements. In particular, we are required to maintain a minimum bid price for our listed ordinary shares of $1.00 per share. If we do not meet these continued listing requirements, our ordinary shares could be delisted. Delisting of our ordinary shares from the Nasdaq Capital Market would cause us to pursue eligibility for

trading on other markets or exchanges, or on the pink sheets. In such case, our shareholders' ability to trade, or obtain quotations of the market value of, our ordinary shares would be severely limited because of lower trading volumes and transaction delays. These factors could contribute to lower prices and larger spreads in the bid and ask prices for our securities. There can be no assurance that our ordinary shares, if delisted from the Nasdaq Capital Market in the future, would be listed on a national securities exchange, a national quotation service, the Over-The-Counter Markets or the pink sheets. Delisting from the Nasdaq Capital Market, or even the issuance of a notice of potential delisting, would also result in negative publicity, make it more difficult for us to raise additional capital, adversely affect the market liquidity of our ordinary shares, reduce security analysts' coverage of us and diminish investor, supplier and employee confidence. In addition, as a consequence of any such delisting, our share price could be negatively affected and our shareholders would likely find it more difficult to sell, or to obtain accurate quotations as to the prices of, our ordinary shares.

Risks Related to Israeli Law and Our Operations in Israel

Our headquarters and other significant operations are located in Israel and, therefore, our results may be adversely affected by political, economic and military instability in Israel.

Our executive offices are located in Tel-Aviv, Israel. In addition, the majority of our officers and directors are residents of Israel. Accordingly, political, economic and military conditions in Israel may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its neighboring countries. Any hostilities involving Israel or the interruption or curtailment of trade between Israel and its trading partners could adversely affect our operations and results of operations. During the winter of 2008-2009, the autumn of 2012 and the summer of 2014, Israel was engaged in armed conflicts with Hamas, an Islamist terrorist organization operating in the Gaza Strip and parts of the West Bank. The last conflict, as well as the previous round of escalation, involved missile strikes against civilian targets in various parts of Israel, including areas in which our employees, service providers and some of our consultants are located. During the summer of 2006, Israel was also engaged in armed conflicts with Hezbollah, a Lebanese Islamist terrorist organization, which also involved missile strikes against civilian targets in the northern part of Israel. The continuation of such strikes may negatively affect business conditions in Israel.

Since February 2011, riots and uprisings in several countries in the Middle East and neighboring regions have led to severe political instability in several neighboring states and to a decline in the regional security situation. Such instability may affect the local and global economy, could negatively affect business conditions and, therefore, could adversely affect our operations. To date, these matters have not had any material effect on our business and results of operations; however, the regional security situation and worldwide perceptions of it are outside our control, and there can be no assurance that these matters will not negatively affect us in the future. In addition, the political and security situation in Israel may result in parties with whom we have agreements involving performance in Israel claiming that they are not obligated to perform their commitments under those agreements pursuant to force majeure provisions in such agreements.

Our commercial insurance does not cover losses that may occur as a result of an event associated with the security situation in the Middle East. Although the Israeli government is currently committed to covering the reinstatement value of direct damages that are caused by terrorist attacks or acts of war, we cannot assure you that this government coverage will be maintained, or if maintained, will be sufficient to compensate us fully for damages incurred. Any losses or damages incurred by us could have a material adverse effect on our business. Any armed conflicts or political instability in the region would likely negatively affect business conditions generally and could harm our results of operations.

Further, in the past, the State of Israel and Israeli companies have been subjects of economic boycotts. Several countries still restrict business with the State of Israel and with Israeli companies. These restrictive laws and policies

may have an adverse impact on our operating results, financial condition or the expansion of our business.

Our operations may be disrupted as a result of the obligation of Israeli citizens to perform military service.

Many Israeli citizens are obligated to perform several days, and in some cases more, of annual military reserve duty until they reach the age of 40 (or older, for reservists who are officers or who have certain occupations) and, in the event of a military conflict, may be called to active duty. In response to increases in terrorist activity, there have been periods of significant call-ups of military reservists. It is possible that there will be military reserve duty call-ups in the future. Our operations could be disrupted by such call- ups, which may include the call-up of our employees or the employees of our Israeli business partners. Such disruption could materially adversely affect our business, financial condition and results of operations.

Exchange rate fluctuations between the U.S. dollar, Euro and the New Israeli Shekel currencies may negatively affect our earnings.

Our functional currency is the U.S. dollar. We incur expenses in U.S. dollars, Euros and New Israeli Shekels, or NIS. As a result, we are exposed to the risks that the Euro and the NIS may appreciate relative to the U.S. dollar, or, if either the Euro and the NIS devalue relative to the U.S. dollar, that the inflation rate in the EU and in Israel may exceed such rate of devaluation of the Euro and the NIS, or that the timing of such devaluation may lag behind inflation in the EU and in Israel. In any such event, the U.S. dollar cost of our operations in the EU and in Israel would increase and our U.S. dollar-denominated results of operations would be adversely affected. The average exchange rate for the year ended December 31, 2015 was $1.00 = Euro 0.82 and $1.00 = NIS 3.88. We cannot predict any future trends in the rate of inflation in the EU and in Israel or the rate of devaluation, if any, of either the Euro or the NIS against the U.S. dollar. As of the date hereof, neither the inflation rate in the EU nor in Israel has exceeded the rate of devaluation of the Euro or the NIS, respectively, during the calendar years 2013, 2014 or 2015.

Provisions of Israeli law and our articles of association, or Articles, may delay, prevent or otherwise impede a merger with, or an acquisition of, our company, which could prevent a change of control, even when the terms of such a transaction are favorable to us and our shareholders.

The Companies Law regulates, among others, mergers, requires tender offers for acquisitions of shares above specified thresholds, requires special approvals for transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to such types of transactions. See "Item 10. Additional Information—B. —"Mergers and Acquisitions under Israeli Law" for additional information

Furthermore, Israeli tax considerations may make potential transactions unappealing to us or to our shareholders whose country of residence does not have a tax treaty with Israel exempting such shareholders from Israeli tax. See "Item 10. Additional Information—E. Taxation—Certain Israeli Tax Considerations" for additional information.

Our Articles also contain provisions that could delay or prevent changes in control or changes in our management without the consent of our Board. These provisions include the following:

- no cumulative voting in the election of directors, which limits the ability of minority shareholders to elect director candidates; and

- the exclusive right of our Board to elect a director to fill a vacancy created by the expansion of the Board or the resignation, death or removal of a director, which prevents shareholders from being able to fill vacancies on our Board.

Anti-takeover provisions in our Articles could make it difficult for our shareholders to replace or remove our current Board and could have the effect of discouraging, delaying or preventing a merger or acquisition, which could adversely affect the market price of our ordinary shares.

Certain provisions of our Articles may have the effect of rendering more difficult or discouraging an acquisition of the Company deemed undesirable by the Board. Those provisions include:

- limiting the ability of our shareholders to convene general meetings of the Company;

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controlling procedures for the conduct of shareholder and our Board meetings, including quorum and voting requirements; and

- the election and removal of directors.

Moreover, the classification of our Board into three classes with terms of approximately three years each, which was approved by shareholders of the Company, the requirement of affirmative vote of at least 75% of the voting rights represented personally or by proxy and voting thereon at a general meeting in order to amend or replace our Articles and the requirement under the Companies Law to have at least two external directors who cannot readily be removed from office, together with the other provisions of the Articles and Israeli law, could deter or delay potential future merger, acquisition, tender or takeover offers, proxy contests or changes in control or management of the Company, some of which could be deemed by certain shareholders to be in their best interests and which could affect the price some investors are willing to pay for our ordinary shares.

It may be difficult to enforce a judgment of a United States court against us, our officers, directors and the Israeli experts named in this annual report in Israel or the United States, to assert United States securities laws claims in Israel or to serve process on our officers, directors and these experts.

We were and continue to be organized in Israel. Substantially all of our executive officers and directors reside outside of the United States, and all of our assets and most of the assets of these persons are located outside of the United States. Therefore, a judgment obtained against us, or any of these persons, including a judgment based on the civil liability provisions of the U.S. federal securities laws, may not be collectible in the United States and may not necessarily be enforced by an Israeli court. It also may be difficult to effect service of process on these persons in the United States or to assert U.S. securities law claims in original actions instituted in Israel. Additionally, it may be difficult for an investor, or any other person or entity, to initiate an action with respect to United States securities laws in Israel. Israeli courts may refuse to hear a claim based on an alleged violation of United States securities laws reasoning that Israel is not the most appropriate forum in which to bring such a claim. In addition, even if an Israeli court agrees to hear a claim, it may determine that Israeli law and not United States law is applicable to the claim. If United States law is found to be applicable, the content of applicable United States 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. As a result of the difficulty associated with enforcing a judgment against us in Israel, our shareholders may not be able to collect any damages awarded by either a United States or foreign court.

Your rights, liabilities and responsibilities as a shareholder will be governed by Israeli law and differ in some material respects from those under U.S. law.

Because we are an Israeli company, the rights and responsibilities of our shareholders are governed by our Articles and Israeli law. These rights, liabilities and responsibilities differ in some material respects from the rights, liabilities and responsibilities of shareholders in a U.S. corporation. In particular, a shareholder of an Israeli company has a duty to act in good faith towards the company and other shareholders and to refrain from abusing his, her or its power in the company, including, among other things, when voting at the general meeting of shareholders on certain matters. Israeli law provides that these duties are applicable to shareholder votes on, among other things, amendments to a company's articles of association, increases in a company's authorized share capital, mergers and interested party transactions requiring shareholder approval. In addition, a controlling shareholder, a shareholder who knows that it possesses the power to determine the outcome of a shareholders' vote or a shareholder who has the power to appoint or prevent the appointment of a director or executive officer in the company, has a duty of fairness towards the company. However, Israeli law does not define the substance of this duty of fairness. Because Israeli corporate law has undergone extensive revisions in recent years, there is little case law available to assist in understanding the implications of these provisions that govern shareholder behavior. These provisions may be interpreted to impose additional obligations and liabilities on holders of our ordinary shares that are not typically imposed on shareholders of U.S. corporations. See Item 10.—B Memorandum and Articles of Association—Shareholder Duties" for additional information

Any of the risk factors referred to above could significantly and negatively affect our business, results of operations or financial condition, which may reduce our ability to pay dividends and lower the trading price of our ordinary shares. The risks referred to above are not the only ones that may exist. Additional risks not currently known by us or that we deem immaterial may also impair our business operations.

ITEM 4. Information on the Company.

Historical Background and Corporate Structure

Our Company, Galmed Pharmaceuticals Ltd., was incorporated in Israel on July 31, 2013 as a privately held company. However, our business has been operating since 2000 under a different group of companies established in the same year, or the Group. Originally, we operated under the parent company, GHI. GHI held all of the equity rights in and to GTTI. GTTI held all of the equity rights in and to GIL (other than 0.1% of the share capital held by GHI). GIL held all of the equity rights in and to GMR. Our intellectual property was held by GIL. The research and development was conducted by GMR as a service to GIL on a cost plus basis. GIL was responsible for all product development.

On February 2, 2014, we underwent the Reorganization, pursuant to which all of our intangible assets (including our intellectual property) are being transferred from GIL to GRD. The Reorganization was effectuated by share transfers and asset transfers, resulting in the Company as the parent company and 100% equity-owner of the following companies: (1) GRD, which holds all the Group's intellectual property, including the Company's patent portfolio; (2) GIL, which may provide research and development services to GRD on a cost plus basis; and (3) GTTI, which is an inactive company that we expect to liquidate during 2016. GIL holds GMR, which became an inactive company in 2015. The Reorganization was conducted in order to simplify our capital structure, reduce our operating cost and to improve our ability to raise funds. Immediately prior to the Reorganization, all our shareholders collectively held 9,739 ordinary shares of GHI. In connection with the Reorganization, and in accordance with the Tax Pre-Ruling, we issued to all such shareholders ordinary shares of the Company, such that upon the Reorganization all our shareholders collectively held 7,099,731 ordinary shares of the Company, in the same proportion among all shareholders, which reflected a ratio of 729 ordinary shares of the Company for each ordinary share of GHI.

The following is a diagram of our corporate structure (assuming GTTI liquidation):

On March 18, 2014, we completed our initial public offering of 3,263,010 ordinary shares at a public offering price of $13.50 per share, which included 425,610 ordinary shares issued upon the exercise in full of the underwriters' option to purchase additional ordinary shares to cover over-allotments, for aggregate gross proceeds of approximately $44.1 million. Net of underwriting discounts, commissions and other estimated offering expenses, the offering raised approximately $39.7 million.

Our principal executive offices and registered office in Israel are located at 16 Tiomkin Street, Tel Aviv, Israel, 6578317 (during 2015, we relocated from our previous address of 8 Shaul Hamelech Blvd., Amot Mishpat Bldg., Tel Aviv, Israel, 6473307) and our telephone number is +972-3-693-8448. Our website address is http://www.galmedpharma.com. The information contained on, or that can be accessed through, our website is neither a part of nor incorporated into this report. We have included our website address in this annual report solely as an inactive textual reference. Puglisi & Associates serves as our authorized representative in the United States for matters concerning our IPO and our registration statement filing on Form S-8 only. Its address is 850 Library Avenue, Newark, Delaware 19711.

Other than as described in “Item 5. Operating and Financial Review and Prospects—Contractual Obligations”, we currently do not have and did not have any material commitments for capital expenditures, including any anticipated material acquisition of plant and equipment or interests in other companies, as of December 31, 2015.

Business Overview

We are a clinical-stage biopharmaceutical company focused on the development of a novel, once-daily, oral therapy for the treatment of liver diseases utilizing its proprietary first-in-class family of synthetic fatty-acid/bile-acid conjugates, or FABACs. We believe that our product candidate, Aramchol, has the potential to be a disease modifying treatment for fatty liver disorders, including NASH, which is a chronic disease that we believe constitutes a large unmet medical need.

Aramchol is a synthetic conjugate of cholic acid, or a type of bile acid, and arachidic acid, or a type of saturated fatty acid, both of which, in their non-synthetic forms, are naturally occurring. The conjugated molecule acts upon important metabolic pathways, reducing fat accumulation in the liver and regulating the transport of cholesterol, which is essential for maintaining cholesterol balance in the body. The ability of Aramchol to decrease liver fat content may also reduce the risk of cardiovascular complications associated with NASH. Independent third-party epidemiologic studies suggest that certain levels of fat reduction may reduce, and ultimately eliminate, liver inflammation in patients who have undergone bariatric surgery or other weight loss programs. We believe that Aramchol’s ability to reduce liver fat without observable adverse side effects in our studies to date will enable it to be a safe and effective treatment for NASH in OD patients and prevent the hepatic and cardiovascular complications associated therewith.

On February 1, 2015, we began our ARREST Study, a multi-center, randomized, double-blind, placebo-controlled, dose-ranging Phase IIB clinical trial of Aramchol, which we intend to conduct in 240 OD patients who have been biopsy-diagnosed as having NASH. We have initiated this study in Israel, Europe, Latin America and in the United States (pursuant to an IND authorized by FDA). Our ARREST Study for Aramchol in OD NASH patients is in accordance with the study design recommended by the Medicines and Healthcare Products Regulatory Agency, or MHRA, and has been deemed acceptable by Bundesinstitut für Arzneimittel und Medizinprodukte, a German medical

agency, or BfArM, and deemed satisfactory by Agence nationale de sécurité du médicament, a French medical agency, or ANSM. The BfArM and ANSM also confirmed, in minutes of each of their respective scientific advisory meetings, that if successful, the ARREST Study may serve as a basis for Phase III pivotal trials of Aramchol. The FDA and MHRA invited us to discuss the next steps in the development of Aramchol after we analyze the results of the ARREST Study. If the Phase III trial(s) are successful, we intend to submit an NDA to the FDA and an MAA to the EMA for the approval of Aramchol for the treatment of NASH in OD patients in the United States and Europe. More information about the ARREST Study may be found on ClinicalTrials.gov identifier: NCT02279524.

Originally, we intended to perform a ‘futility analysis’ as part of the ‘interim analysis.’ The futility analysis would have reviewed the data both for safety signals and determined whether subjects receiving Aramchol showed an observable reduction in liver fat concentration, as measured by MRS. The independent Drug and Safety Monitoring Board (DSMB) would have then made a “go/no go” decision based on the MRS data at six months. The absence of significant MRS-related results at the six month point could have resulted in the termination of the study based on the absence of clinical benefit in the interim review and was therefore considered a futility analysis.

However, in light of the FDA and AASLD clinical guidance for the development of diagnostic and therapeutic modalities for the treatment of NASH published in early 2015, it has become increasingly clear that histological data (liver biopsy) will be absolutely required to seek regulatory approval for NASH drugs, not merely MRS data. This conclusion was further supported by two recent Phase III protocols (the REGENERATE Study, NCT02548351, and RESOLVE-IT study- NCT 02704403), which also require resolution of NASH as measured by histological data. As such, the entire twelve month dataset will be necessary to judge the viability of Aramchol, and potential further development thereof.

Thus, the scope of the interim analysis we are currently planning on conducting once 120 patients in our ARREST Study complete six months of treatment, will be limited to analysis of safety related signals only, conducted by the DSMB. The interim analysis will not include review of the data with respect to any efficacy endpoints.

The DSMB will decide whether to continue studying both doses or move all patients to one dose, if one is found to be safer than the other. We do not anticipate the interim results to lead to the stoppage of our ARREST Study, but no assurance can be given. We currently expect results from the interim analysis to be completed by December 2016, or early first-quarter 2017 and top-line data for the ARREST Study to be completed in the first quarter of 2018, inclusive of the three-month follow-up period.

Non-Alcoholic Fatty Liver Disease (NAFLD) / Non-Alcoholic Steato-Hepatitis (NASH)

It is currently estimated that Non-Alcoholic Fatty Liver Disease (NAFLD), the precursor condition to NASH, could affect up to 30% of the adult population in developed countries. This disease is also now recognized as one of the most common liver disorders, and a significant and growing public health problem. In the US alone, more than 100 million people are said to be affected by NAFLD, and its prevalence is rapidly growing in parallel with metabolic syndromes, particularly obesity and diabetes.

NAFLD is characterized by the accumulation of fat of 6% or greater in the liver of people who drink alcohol only in moderation, or not at all. There may be numerous causes of NAFLD, however, the disease is mostly associated with a high fat, fructose-rich diet. Although NAFLD is generally asymptomatic, it is a major risk factor for liver inflammation (NASH) and scarring (fibrosis and cirrhosis). In addition, NAFLD is also associated with metabolic syndrome and cardiovascular disease. Currently, NAFLD can only be managed through lifestyle improvements, such as weight reduction and physical activity.

NASH is currently estimated to affect between 4%-6% of the adult population in developed countries, and is associated with increased risk of liver cirrhosis, liver failure, hepatocellular cancer, as well as metabolic and cardiovascular diseases. The major characteristics of NASH are elevated liver fat along with inflammation and fibrosis.

However, despite the growing need, there are currently no approved therapeutic treatments for NASH. Modification of risk factors, such as obesity and hyperlipidemia, and proper diabetic control is generally recommended for the treatment of NASH, and the standard of care includes lifestyle changes to promote weight loss, including low-calorie,

low-fat diets and physical activity. Although weight loss can be potentially significant in delaying the progression of NASH, studies have shown that, for most individuals, it is generally very difficult to maintain over the long-term, even following bariatric surgery.

There are currently no drugs approved by regulatory authorities for the treatment of NASH. Even though certain drugs, such as insulin sensitizers and antihyperlipidemic agents, are prescribed for some NASH patients, they are not approved for the treatment of NASH and their efficacy has not been proven in adequate and well-controlled clinical studies. Such prescription or use of unapproved drugs is typically known as “off-label” prescription or use. In particular, the anti-diabetic drug, Metformin®, is used for patients who have type 2 diabetes (T2DM) as well as NASH. Other drugs such as Orlistat (Xenical®, Roche) and Glitazones are sometimes used for non-diabetic NASH patients, however their long term safety and efficacy in NASH patients has not been established. Bariatric surgery can be performed in obese patients with NASH, but is not an established procedure to treat NASH. Lastly, vitamin E was found to be beneficial for non-diabetic patients with biopsy-proven NASH, but not for diabetics with NASH, NAFLD or liver cirrhosis. As such, the use of vitamin E is fairly limited.

Currently, it is impossible to predict which of the NAFLD patients will deteriorate to NASH as it is unclear what causes NASH to develop. Researchers are now focusing on several factors that may contribute to the development of NASH. Therefore lifestyle changes are recommended for all patients with NAFLD.

In 2015, the FDA and AASLD issued clinical guidance for the development of diagnostic and therapeutic modalities for the treatment of NASH based on the joint workshop held on September 5-6, 2013. The guidance serves as a broad framework for discussions with different companies and the requirements for pivotal studies for receiving regulatory approval are decided case-by-case depending on the products profile and previous studies results.

There is an exceptionally wide range of estimates regarding the size of the commercial market for NASH. This uncertainty stems from (i) the overall size of the patient population, (ii) the percentage of the addressable market that will be diagnosed and, subsequently, seek treatment, and (iii) the ultimate cost of the therapies. None of these factors can be known definitively until NASH drugs begin to hit the market, which based on analysts' estimates, will likely be 2019 at the earliest. Independent estimates generally estimate a commercial market in excess of $10 billion in developed countries, though we do not endorse any estimates, which are based on a number of different underlying assumptions.

Aramchol for NASH

Overview

Our product candidate, Aramchol, is a first-in-class synthetic FABAC which we are initially developing for the once-daily oral treatment of NASH in OD patients.

Early in its development, Aramchol's ability to modulate hepatic lipid metabolism was observed and validated in numerous preclinical trials with different animal species. Mice fed a high fat diet and treated with Aramchol did not develop fatty liver. In contrast, fatty liver was observed in control mice fed a high fat diet but not treated with Aramchol. In such early studies, we also observed that the mechanism of this effect was not a result of malabsorption of fat in the intestines because the FABAC-treated mice gained weight throughout the test periods to a similar degree to the control mice. This led us to conclude that FABAC therapy triggers a beneficial modulation of intra-hepatic lipid metabolism and thus reduces liver fat content. The images below show the reduction of liver fat content in rodents after treatment with Aramchol.

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In *in-vitro* studies, Aramchol partially inhibited the Stearoyl-Coenzyme A Desaturase-1, or SCD1, enzyme, an enzyme recognized as playing an important role in the metabolism of fatty acids. The SCD1 enzyme is essentially the gateway that regulates the use and storage of fat in the body by converting saturated fatty acids to monounsaturated fatty acids. Experimental animal studies showed that complete inhibition of the SCD1 enzyme protects against diet-induced obesity, hepatic steatosis, or fatty liver, and insulin resistance by instructing the body to use, rather than store, all fatty acids. However, various animal studies have indicated that such complete SCD1 enzyme inhibition has serious side effects, such as inflammation, atherosclerosis and pancreatic beta cell dysfunction. As observed by us in our pre-clinical and clinical studies performed to date, and subsequently published in the European Journal of Gastroenterology and Hepatology and Archives of Medical Research in 2008 and 2010 respectively, one of Aramchol's unique characteristics is that it triggers a partial SCD1 enzyme inhibition and, to date, we have not observed any significant adverse events in our clinical studies.

Aramchol also has the ability to up-regulate ABCA1 and thereby induce "reverse cholesterol transport" in animal models. ABCA1 is an ATP-binding cassette transporter, also known as the cholesterol efflux regulatory protein (CERP), which is a regulator of cellular cholesterol and phospholipid homeostasis. In every cell of the body, the LDL receptor enables entry of cholesterol into the cell and the ABCA1 transporter pumps cholesterol out of the cell, where it is carried by high-density lipoprotein, or HDL, to the liver to be excreted into the intestine. This pathway of cholesterol from the cell to the liver is called reverse cholesterol transport and is essential for maintaining cholesterol balance in the body. Excess LDL, or "bad," cholesterol is deposited mainly in vascular walls, causing atherosclerosis, a vascular disease in which an artery wall thickens as a result of the accumulation of calcium and fatty materials, such as cholesterol. Activation of reverse cholesterol transport reduces the bad cholesterol deposited in vascular walls and is therefore beneficial. As published in the Biochemical Journal, the Archives of Medical Research and the Current Opinion in Lipidology in 2006, 2010 and 2014, respectively, in several experimental models in animals, Aramchol has been shown in independent studies to increase ABCA1 activity by between 300% and 400%, thereby stimulating reverse cholesterol transport, reducing cholesterol levels and preventing atherosclerosis. An article in the April 2014 issue of Biochimie further supports the importance of the regulation of ABCA1-induced reverse cholesterol transport on the pathogenesis of NASH.

Additional Preclinical and Clinical Studies Required for Regulatory Submissions

The tolerability of Aramchol has been demonstrated in toxicity studies performed in rats (up to six months) and dogs (up to nine months), as well as reproductive studies in rats and rabbits. More recently, we conducted a food effect and PK study in 66 healthy volunteers to evaluate the PK of Aramchol following single and multiple escalating doses as well as to evaluate the effect of a high-fat, high-calorie meal on the PK of Aramchol following a single dose in healthy volunteers.

The results showed dose-related, but less than dose-proportional, increases in the mean Aramchol plasma concentrations, or Cmax, area under the curve, or AUC (0-t), and AUC (inf) of 200 mg, 400 mg and 600 mg doses administered under fasting conditions or following a light meal, both at single and repeated dose administration. Cmax and AUC are metrics used to indicate the significance of a drug's exposure. Steady-state was achieved by 144 hours

(day seven). Administration of Aramchol after a high-fat, high-calorie meal afforded a 2.6 fold increase in exposure, as measured by Cmax, AUC(0-t), and AUC(inf) compared to the fasting group.

No serious adverse events or deaths occurred during the study and only one patient withdrew due to an adverse event, which was categorized as unrelated to Aramchol. Of the 27 adverse events reported in the study, 24 were considered to be unrelated to Aramchol and three, all of which were mild, were considered to be possibly related. No clinically significant abnormalities related to any Aramchol dose were noted in ECGs, laboratory results, vital signs or physical examinations.

To date, we have successfully completed four clinical trials of Aramchol:

- **A Phase 1 Single and Multiple-Dose Study of Aramchol in Healthy Male Volunteers (NCT00776841):** This study was performed in two parts: (a) a single dose, double-blind, placebo-controlled, Phase IA study with ascending doses of Aramchol in healthy volunteers in one center in Israel, in which no serious adverse side effects were observed; (b) a Phase IB repeated-dose trial in healthy volunteers in one center in Israel, in which no adverse side effects were observed and which confirmed the suitability of a once-daily dose of Aramchol.

- **Study of Aramchol in Patients With Fatty Liver Disease or Nonalcoholic Steatohepatitis (NCT01094158)**: Thereafter, we commenced a multi-center, randomized, double-blind, placebo-controlled Phase IIA trial of Aramchol in 60 NAFLD and NASH patients in 12 centers in Israel. This study, whose design was deemed acceptable by the FDA in 2007 at a pre-IND meeting suggested that Aramchol reduced liver fat in a dose-dependent manner, as evidenced by a statistically significant reduction of liver fat over a three month treatment period of once-daily 300 mg doses of Aramchol, and induced positive trends of changes in several metabolic parameters. Based on these Phase IIA proof-of-concept results, we established a development plan that we believe may confirm that Aramchol (i) is safe, (ii) can be administered as a once-daily oral therapy, (iii) targets NASH, (iv) can effectively treat inflammation and thus prevent the progression of NASH and (v) can treat metabolic syndrome, the underlying condition of NASH, by improving parameters of metabolic syndrome including insulin resistance and homeostatic model assessment, or HOMA, levels, which are used to quantify the metabolic syndrome biological marker insulin resistance and beta-cell function, and adiponectin levels.

- **Pharmacokinetics of Single and Multiple Escalating Doses of Aramchol and Food Effect in Healthy Volunteers (NCT02374437)**: On April 28, 2014, we commenced PK and food effect studies of Aramchol. In written correspondence from December 2013 regarding a requested pre- IND meeting, the FDA recommended that we conduct such studies prior to commencing our Phase IIB ARREST Study. We conducted the PK study at the Sourasky Medical Center in Tel Aviv, Israel. We enrolled 66 healthy male volunteers who received three doses of Aramchol: 200 mg, 400 mg and 600 mg. The two higher doses are being used in our ARREST Study. In December 2014, we completed the statistical analysis of the PK study of the three doses of Aramchol and observed no serious adverse events. The PK study provides additional safety data to further support existing safety data from our pre-clinical studies and our Phase I and Phase IIA clinical trials of Aramchol.

Phase I Trials

Aramchol was evaluated in two Phase I clinical trials to study its safety, tolerability and PK profile in healthy volunteers, in both single and multiple dose administrations. The first Phase I clinical trial was an escalating single-dose trial conducted in 16 subjects testing Aramchol doses ranging from 30 mg to 900 mg. The subsequent Phase I clinical trial was a repeated-dose trial conducted over four days in 25 subjects testing repeated daily doses of Aramchol of 30 mg and 300 mg. The profiles for the groups were similar and the maximal plasma concentration of Aramchol increased with the higher doses. The PK profile demonstrated that Aramchol is suitable at each dose for once-daily administration and there were neither significant adverse events observed in either Phase I trial nor any notable changes in biochemical, hematologic, cardiovascular or other safety parameters.

Phase IIA Trial: Aramchol Treatment in NAFLD or NASH Patients

In January 2012, we completed a 60 patient multi-center, randomized, double-blind, placebo-controlled Phase IIA clinical trial of Aramchol in patients with NAFLD or NASH between the ages of 18 and 75 in 12 centers in Israel. The Phase IIA study results were published in July 2014 in the peer-reviewed Clinical Gastroenterology and Hepatology Journal. In accordance with the AASLD's guidelines for Phase IIA studies in NAFLD or NASH, the trial was

performed in patients with either NAFLD or NASH, rather than only in NASH patients. The trial's primary efficacy endpoint was a reduction in liver fat content, and did not consider inflammation or fibrosis, which can be diagnosed only by liver biopsy. We believe that the short study duration of three months of treatment followed by a one-month follow-up period did not warrant repeated biopsies. The trial evaluated the effects on liver fat content of 100 mg and 300 mg once-daily doses of Aramchol compared to a placebo. At the end of the three month treatment period, statistically significant reductions in liver fat concentration as measured by MRS were observed in the 300 mg patient group. Specifically, a 12.57% mean liver fat content reduction was observed in the 300 mg group, as compared to a mean reduction of 2.89% in the 100 mg group and a mean increase of 6.39% in the placebo-treated patients. These results indicate that the effects of Aramchol are dose-dependent, as demonstrated in the graph below, which presents the results with respect to the 57 patients who successfully completed the entire treatment period.

Relative Change in MRS from Baseline after Three Months of Treatment

The difference between baseline and liver fat concentration at the end-of-treatment, as measured by MRS, for patients diagnosed with NASH and with NAFLD is presented in the following table, which also presents the results with respect to the 57 patients who successfully completed the entire treatment period (three patients were excluded from data analysis because of protocol violations).

Relative Change in Liver Fat Concentrations in the NASH and NAFLD Groups

Liver MRS	**Aramchol 300 mg/d Mean ± SD**	**Aramchol 100 mg/d Mean ± SD**	**Placebo Mean ± SD**
NASH	-35.42 ± 50.09 (N=2)	-9.82 ± 4.57 (N=2)	19.24 ± 29.69 (N=2)
NAFLD	-10.03 ± 18.22 (N=18)	-6.05 ± 26.10 (N=16)	4.88 ± 37.44 (N=17)

N = number of patients

SD = standard deviation

The graph and table above show that the primary endpoint of the study was attained. The study demonstrated a statistically significant, dose dependent reduction in fat content in the livers of patients treated with Aramchol, with a 19% difference between the 300 mg dose group and the placebo group, while the difference between the 100 mg dose group and the placebo group was not statistically significant.

A non-statistically significant change of approximately 1 Kg in body weight was observed between the 300 mg dose group and the placebo group, suggesting that weight-loss did not influence the observed reduction in liver fat content experienced in the Aramchol treated groups.

In addition, both treated patients and the placebo group showed a trend of reduction in alanine aminotransferase, or ALT, levels, which is a marker of hepatocellular injury and an indicator of liver disease. The Aramchol treated groups' ALT values relapsed 30 days post-treatment, indicating that after the cessation of Aramchol treatment, the patients experienced recurring liver inflammation. The placebo group did not demonstrate a relapse in ALT levels. This supports the supposition that Aramchol has a real biological effect.

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Total cholesterol and LDL cholesterol levels were determined as safety parameters in our Phase IIA study. Differences between low-dose Aramchol (100 mg/d), high-dose Aramchol (300 mg/d) and the placebo were also analyzed for secondary efficiency endpoints. The graphs below show no statistically significant differences among the three treatment groups for cholesterol and LDL.

Adiponectin is a protein that modulates metabolic processes, including the regulation of glucose levels and fatty acid breakdown in the body. Adiponectin has an anti-inflammatory and antifibrotic effect on the liver. Adiponectin deficiency, or low amounts of adiponectin, results in insulin resistance, glucose intolerance, abnormal levels of fat in the blood and vascular injury, all of which are characteristic of metabolic syndrome. The graph below shows the change in serum adiponectin levels from baseline during treatment. At the end of the three month treatment period, a non-statistically significant increase in serum adiponectin levels were observed in the Aramchol treated patient groups, indicating that Aramchol increases serum adiponectin levels in a dose dependent manner, suggesting that Aramchol may act as a protective factor for the prevention of metabolic syndrome, as increased serum adiponectin is itself such an independent protective factor.

Change in Serum Adiponectin Levels from Baseline during Three Months of Treatment

The arterial endothelium is a target for the atherosclerotic process. Atherosclerosis is associated with endothelial dysfunction in the very early stages of the disease process. Several studies have shown that metabolic syndrome is associated with endothelial dysfunction as an early pathogenic event. Thus, assessing endothelial function serves as an early marker for both metabolic syndrome and atherosclerosis. In the present study, endothelial function was assessed using flow-mediated dilation, a noninvasive ultrasound-based method that measures the ability of a large conduit artery to dilate in response to a shear stress stimulus, or an external force acting on the blood vessel. At the end of the three month treatment period, a non-statistically significant improvement in endothelial function was observed in the 300 mg Aramchol treated patient group. The table and graph below present the change in endothelial function, as measured by flow mediated dilation observed between baseline and the end-of-treatment for the 48 patients who performed two flow mediated dilation examinations.

Change in Endothelial Function between Baseline and the End-of-Treatment

	Aramchol 300 mg/d	Aramchol 100 mg/d	Placebo
FMD (mm Hg)	Mean ± SD	Mean ± SD	Mean ± SD
	N=20	N=18	N=19
Pre-treatment	4.6 ± 2.5	5.4 ±2.8*	6.4 ±2.9
Post-treatment	5.9±2.1	5.7±3.9	6.6±2.3
Change	1.28±2.92	0.27±3.42	0.23±2.42
P value**	0.453	0.8979	

N = number of patients

SD = standard deviation

* N = 16 for this data point.

** P value is determined according to an analysis of covariance using the Dunnett method, or a multiple comparison method, for the difference between treatment group and placebo, adjusted for age, gender, diagnosis, baseline

HbA1c and baseline weight.

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The improvement in endothelial function suggests a positive effect on metabolic syndrome, specifically on vascular function.

Furthermore, there were no notable changes in biochemical, hematological, cardiovascular or other safety parameters, and there were no serious drug related adverse events in the Aramchol treated group during the three month treatment period or the subsequent recovery period. Aramchol's adverse event profile was comparable to that of the placebo, as portrayed in the chart below.

The results of our Phase IIA clinical trial of Aramchol in the peer-reviewed Clinical Gastroenterology and Hepatology Journal were published in December 2014. The trial manuscript, entitled "The Fatty Acid-Bile Acid Conjugate Aramchol Reduced Liver Fat Content in Patients with Nonalcoholic Fatty Liver Disease," provides the full report of the Phase IA trial, which was completed in January 2012 and presented at the 47th Annual Meeting of the European Association for the Study of the Liver in 2012.

Chronic Toxicology studies

Since the completion of the Phase IIA study, additional non-clinical chronic toxicology studies have been conducted in pharmacologically-relevant species to support the initiation of our ongoing ARREST Study and planned Phase III clinical studies. These studies were performed in compliance with the EMA's ICH M3 (R2) guidelines by WIL Research, a global contract research organization, at its facility in Holland. The studies are required in advance of the commencement of human clinical trials and marketing authorization for pharmaceuticals in Europe and the United States. The toxicity program for Aramchol included repeat dose studies of up to six months in rats and up to nine months in dogs by oral administration, the intended clinical dose route. These studies demonstrated that Aramchol was well-tolerated at the dose levels investigated with no-observed-adverse-effect-level, or NOAEL, values of 1000 mg/kg/day in rats and 1500 mg/kg/day in dogs, the maximum feasible dose in both species. There were no observations noted in the rat study. The findings in the dog study were limited to changes in plasma lipids, including decreases in total blood cholesterol levels, LDL, HDL and phospholipids, and a slight increase in the size of the adrenal glands, which were considered to be an extension of the primary pharmacology of Aramchol and non-toxic effects, and skin scales from week 13 onwards in all Aramchol-treated groups, with a dose-related incidence. The decrease in total blood cholesterol levels in the dog study further supports our understanding of the positive effect of Aramchol on lipids as we previously observed in our preclinical studies in other animals. After six months this was not accompanied by any microscopic alteration of the skin and therefore considered not toxicologically relevant. Results from the study show that after nine months the presence of scales in all Aramchol-treated groups was accompanied by minor test item-related microscopic findings in the skin: Hyperkeratosis of the epidermis, correlating to the scales, and keratin plugs in the hair follicles (in males at 750/500 and 1500 mg/kg). After a 12-week treatment-free recovery period, fewer scales were noted and microscopically there was partial recovery. As these findings were minor and no clinical symptoms like scratching were noted, these findings were considered not adverse.

Aramchol was non-mutagenic in vitro in the Ames test and chromosomal aberrations test, each of which is a test to determine whether the subject chemical can cause mutations in the DNA of an organism. In addition, in bone marrow micronucleus test in male rats at a 2000 mg/kg oral dose (the maximum recommended dose in accordance with ICH S2 (R1)), Aramchol was not clastogenic, meaning it did not give rise to or induce disruption or breakages of chromosomes, nor was it aneugenic, meaning it did not cause the number of chromosomes in the nucleus of a cell to not be an exact multiple of the monoploid number of a particular species.

Embryo-fetal development toxicity was assessed in rats and rabbits. No maternal or fetal development toxicity was observed in either species. The NOAEL for maternal and development toxicity was at least 1000 mg/kg in rats and 750 mg/kg in rabbits (the maximum feasible dose in both species).

No maximum tolerated doses were reached in the studies. A 50-fold safety margin exposure multiple was achieved in dogs but not in rats. However, for rats, at least three of the four ICH M3(R2) safety margin criteria were met, and for dogs all four criteria were met. Blood tests revealed a decrease in total blood cholesterol levels, including LDL, HDL and phospholipids, and there was a slight increase in the size of the adrenal glands of the dogs, which WIL Research assessed as a physiologic compensatory response to the decrease in blood cholesterol levels. WIL Research did not

consider the decrease in blood cholesterol levels or the physiologic response of the adrenal glands as a toxic effect, but rather as a pharmacodynamic effect, which is a biochemical and physiological effect of the drug on the body. Based on the above, WIL Research concluded that the overall safety data for Aramchol is sufficient to support the proposed Phase IIB clinical trial.

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Summary of Aramchol Clinical Trials

Our Phase IIB ARREST Study for Aramchol

The Company believes that Aramchol will reduce and eventually eliminate liver inflammation by the mechanism of action described above, while also mitigating cardiovascular comorbidities.

We submitted an IND application to FDA to initiate the ARREST Study, and hope to expand the scope of the IND in the future to conduct pivotal Phase III clinical trials for NASH and other clinical trials in the United States. The FDA cleared our IND application, allowing us to conduct the Phase IIB ARREST Study in the United States. In September 2014, the FDA granted Fast Track designation status to Aramchol for the treatment of NASH. Fast Track designation may accelerate the development process and may expedite the review of drugs that show promise in treating serious, life-threatening medical conditions for which no other drug either exists or is as effective.

We are currently conducting our Phase IIB ARREST Study to evaluate the safety and effectiveness of two different doses of Aramchol for the treatment NASH in OD patients. In order to be eligible to participate in our ARREST Study, patients must be affected by NASH, as diagnosed by a biopsy, be overweight as measured by a Body Mass Index between 26 and 29 or obese as measured by a Body Mass Index of 30 or greater, and who are pre diabetic or type II diabetic. We target this specific population as it is at the greatest risk of developing the complications that are associated with NASH. Although based on the identified mechanism of action of Aramchol we do not expect an effect on liver fibrosis, we included patients with and without liver fibrosis in the trial, as such an effect may occur mediated by the reduction in inflammation or resulting from another, yet unidentified mechanism of action. Patients are randomized into one of three trial groups taking either one of two different once-daily oral doses of Aramchol or a placebo. The treatment part of the trial is designed to be 12 months in duration and patients completing this phase will be observed for a three month follow-up period. This trial is designed to enroll 240 patients (89 patients in the 400 mg Aramchol group, 89 patients in the 600 mg Aramchol group and 62 patients in the placebo group) across approximately 70 clinical sites in the United States, Europe, Latin America and Israel.

The primary endpoint of the 12-month double-blind portion of the trial is a statistically significant reduction in liver fat concentration as measured by MRS, which is a surrogate endpoint that is generally accepted by the FDA with respect to Phase I and Phase II NASH studies.

Secondary endpoints of the trial include a resolution of NASH (currently defined as disappearance of ballooning), as measured by liver biopsy, with no worsening of fibrosis. Other secondary endpoints are improved liver and metabolic biomarker levels and exploratory endpoints, such as blood liver enzymes and metabolomics. The Company believes that finding a non-invasive test that correlates well with biopsy findings would significantly increase the likelihood of the future use of Aramchol in an outpatient setting, where biopsies, which are expensive and subject the patient to risk and discomfort, are not generally used to diagnose NASH.

In communications received in response to our submission of an update to our IND in 2014, FDA recommended that future clinical studies should be discussed at an end-of-Phase II meeting, which could take place within three months from the date we complete the analysis of the results of our ARREST Study, and at which time the trial results could be considered. The FDA communication further noted that we must discuss with the FDA a methodology for our drug development processes as our development of Aramchol progresses in order to determine which surrogate endpoints, if any, the agency will accept to demonstrate the efficacy of Aramchol for the purposes of NDA approval. In light of the publication of the FDA and AASLD joint workshop guidance, and based on the Phase III trial designs published to date by other companies drugs for NASH, we currently believe that we will likely be approved if the end points of the pivotal study are met, but FDA may require as a condition of approval that we complete a Phase IV, post-approval, study assessing effectiveness based on morbidity and mortality endpoints (e.g., reduction in deaths and other significant clinical events), as well as evaluating safety. The failure to successfully complete any required post-market study could result in FDA withdrawing approval for Aramchol.

Potential Phase III Program for Aramchol

The development work we have completed to date with regard to Aramchol was deemed appropriate for the initiation of a Phase IIB study by the MHRA, BfArM and ANSM, in addition to FDA as noted above. Our ARREST Study design is in accordance with the study design recommended by the MHRA, deemed acceptable by BfArM and deemed satisfactory by ANSM. BfArM and ANSM also confirmed, in minutes of each of their respective scientific advisory meetings, that, if our ARREST Study is successful in reaching its primary endpoint, we may proceed to pivotal randomized, double-blind, placebo-controlled, Phase III trials. We expect the primary endpoints of such trials to be the resolution of NASH as evidenced by disappearance of ballooning and some reduction in inflammation. Like FDA, as noted above, the MHRA invited us to discuss the next steps in the development of Aramchol after we complete the analysis of the results of our ARREST Study, at which time the data from the study will be considered.

Aramchol for the Treatment of Other Indications

In addition to the ARREST Study, we are exploring other indications for the use of Aramchol.

On December 1, 2015 we announced that our Investigational New Drug (IND) for the ARRIVE Study, a proof-of-concept clinical trial that will evaluate the safety and efficacy of Aramchol in up to 50 patients with HIV-associated lipodystrophy and NAFLD, was allowed by FDA to proceed. The ARRIVE Study is an investigator-initiated study sponsored by the University of California San Diego, where it will be conducted, and led by Professor Rohit Loomba. The Study is designed as a randomized, double-blinded, allocation-concealed, placebo-controlled, proof-of-concept Phase IIA clinical trial, and will evaluate either Aramchol at 600 mg or placebo for 16 weeks in up to 50 patients with HIV-associated lipodystrophy and NAFLD. Pre- and post-treatment MRI-measured liver fat content and total body fat via dual energy x-ray absorptiometry (DEXA) will be compared. The primary end point of successful therapy will be an improvement in hepatic steatosis as measured by MRI. Secondary endpoints will be an improvement in total body fat, metabolic profile, and liver biochemistry. On March 1, 2016, we announced that we have randomized the first patient in the ARRIVE study. We believe that top line results will be available by the end of 2017.

HIV is a major global health issue, with 35.3 million people living with the disease worldwide, 2-3 million of whom are in the United States and Western and Central Europe. While effective combination antiretroviral therapy (cART) has resulted in a major reduction in acquired immunodeficiency syndrome (AIDS)-related mortality overall, liver disease is now the second leading cause of death in patients with HIV, accounting for nearly 7-14% of all deaths in this population. The prevalence of NAFLD is higher in individuals with HIV infection than in the general population. A recently conducted clinical trial at the University of California San Diego by Professor Rohit Loomba, the largest such study to-date, compared age- and sex-matched patients with primary NAFLD, with patients with HIV-associated NAFLD, and found that patients with HIV-associated NAFLD had significantly higher rates of definite steatohepatitis (63% vs. 37%, P = 0.04), and more features of liver injury.

On November 13, 2014, we announced the first administration of Aramchol in a proof-of-concept Phase IIA clinical trial for the treatment of newly formed cholesterol gallstones following bariatric surgery. However, due to poor patient recruitment and higher-priority clinical programs, we decided to terminate the study on October 1, 2015. At the moment, we believe that it is unlikely that we will revive another study in cholesterol gallstones.

We are also investigating the possibility of developing combination therapy to address NASH-associated fibrosis. Such product could potentially combine Aramchol with either a new compound that would be developed in house, with an existing compound that has undergone pre-clinical testing and which we would license from a separate entity or with an existing compound we will reposition. We plan to announce developments in combination therapy for advanced (fibrotic) NASH in the second quarter of 2016.

Our Competitive Strengths

The pharmaceutical industry is characterized by rapidly evolving technology, intense competition and a highly risky, costly and lengthy research and development process. Adequate protection of intellectual property, successful product development, adequate funding and retention of skilled, experienced and professional personnel are among the many factors critical to success in the pharmaceutical industry. We believe Aramchol is strategically positioned to address the unmet medical needs of OD patients with NASH. Our competitive strengths include:

- **A once-daily oral drug without observable adverse side effects to date in development for the chronic treatment of OD patients with NASH**. We believe that the characteristics of Aramchol, including its ability to reduce liver fat content without observable adverse side effects in our studies to date, which we believe may result in an anti-inflammatory effect, its ability to modulate the transport of cholesterol in the body and simple and convenient delivery through once-daily oral administration, position it well against the competition in the treatment of NASH. We believe that such characteristics may also lead to Aramchol's acceptance and adoption by the medical community and patients as an alternative to the medical treatments used today, which are not approved by applicable regulatory authorities for treatment of NASH as their efficacy has not been proven in adequate and well-controlled clinical studies. We believe Aramchol is well-positioned against drugs in development for NASH, some of which may

require intravenous delivery or may cause adverse events, such as itching or an increase in LDL, which can be highly inconvenient for patients with chronic diseases, such as NASH, and may result in low patient compliance.

Extensive knowledge and expertise in the treatment of liver diseases, the development of FABACs and working with lipid molecules. We believe our management team, scientific advisors and personnel have extensive knowledge and experience in the treatment of liver diseases, developing FABACs, such as Aramchol, for the treatment of liver diseases and working with lipid molecules, which due to their special physiochemical characteristics, are difficult to synthesize, develop and work with. We believe that such knowledge and expertise makes us competitive in the metabolic and liver diseases.

Ability to target Pre Fibrotic NASH and observed metabolic effect. On September 29, 2014, we purchased 60 EndoPAT™ devices and accessories from, and entered into a collaboration with, Itamar Medical LTD., or Itamar, to include an assessment of endothelial, or arterial, function in our Phase IIB ARREST Study. In the completed Phase IIA study we observed a trend of improvement in endothelial function in patients treated with 300 mg of Aramchol. The EndoPAT™ device will allow for a validated, consistent measurement of endothelial function in patients participating in the study. As mentioned, NASH patients develop cardiovascular complications and present with endothelial dysfunction as a marker of their propensity for atherosclerosis, or hardening of the arteries. A significant improvement in endothelial function, if found, will provide an additional advantage for patients treated with Aramchol and will be a differentiating factor for Aramchol among other NASH drugs in development.

- **Non-invasive diagnostic tools for NAFLD/NASH and the assessment of Aramchol's therapeutic responses.** On July 8, 2015, we announced that we entered into a Research, Option and License Agreement and a Share Purchase Agreement with One Way Liver Genomics S.L., or OWL, which developed the proprietary OWL LIVERTest®, a test seeking to stratify NAFLD and NASH patients according to their metabolic profile. Under the License Agreement, we and OWL will work together during our ARREST Study to develop a non-invasive blood test including metabolic markers that could potentially predict therapeutic responses to Aramchol. The development of this proprietary non-invasive complementary diagnostic for Aramchol could replace liver biopsy in testing the ongoing efficacy of treatment, which may enhance Aramchol market penetration.

We hope that our efforts will lead to the identification of specific biomarkers, which will differentiate NASH from NAFLD patients without the need for liver biopsy, and serve as a tool for the prediction and assessment of Aramchol's efficacy. The identification of such specific biomarkers may greatly improve Aramchol's chances of qualifying for reimbursement from third-party payors, by providing an indication of the patients who are most likely to benefit from treatment with Aramchol.

Our Strategy

Our strategy is to build a specialized biopharmaceutical company that discovers and develops novel FABAC drugs and potentially other molecules for the treatment of liver diseases, beginning with the treatment of fatty liver disorders, primarily NASH, and potentially other metabolic disorders. We focus on drugs and drug conjugates for liver diseases with global market potential and we seek to create global partnerships with academic institutions and biotechnology or pharmaceutical companies to effectively assist us in developing our portfolio and ultimately commercializing our products. Through this approach, we have successfully advanced Aramchol into various stages of clinical development. Key elements of our strategy include:

- **Continuing to advance the development of Aramchol for the treatment of NASH**. Our development of Aramchol for treatment of NASH currently includes our ongoing Phase IIB ARREST Study. If this study is successful, the results will serve as a basis for potential Phase III pivotal trial(s) in the United States, Latin America, Europe and Israel for the same indication. Assuming successful completion of Phase III trial(s), which could be carried out by us in conjunction with a strategic partner under a licensing agreement, we intend to seek regulatory approval of Aramchol in the United States and Europe for the treatment of NASH in OD patients.

- **Exploring other indications for the use of Aramchol**, which includes the ARRIVE Study, a proof-of-concept Phase IIA clinical trial that will evaluate the safety and efficacy of Aramchol in up to 50 patients with HIV-associated lipodystrophy and NAFLD. We expect to announce additional clinical trials during the course of 2016.

- **Establishing a development and commercialization partnerships for Aramchol before the completion of the ARREST Study in geographies outside of our main territorial focus.** Forging development and commercialization partnership(s) outside our main territorial focus of the United States, Europe and Israel, through

out-licensing agreements with pharmaceuticals or biotechnology companies that possess experience, resources and infrastructure to execute a successful market launch and provide sales support for Aramchol in the licensed territories. Such potential partnerships could be sought before the completion of the ARREST Study.

- **Establishing a global development and commercialization partnership for Aramchol upon completion of the ARREST Study or after the successful completion of the first of the potential Phase III trials of Aramchol for the treatment of NASH**. Following the successful completion of the ARREST Study, which we provide no assurance we will achieve, we intend to out-license Aramchol to a multinational pharmaceutical company that possesses experience, resources and infrastructure to execute pivotal trial(s), regulatory approval and market launch.

- **Advancing existing collaborations, and seeking additional partnerships, for the discovery and validation of diagnostic tools and biomarkers for the diagnosis of liver disease**. We intend to advance our existing collaborations and strategic arrangements for the discovery and validation of non-invasive diagnostic tools and biomarkers for the diagnosis of liver disease, including NASH. We are currently collaborating with OWL, on the development of a non-invasive biomarker, which, if successful, may help to predict individual responses to Aramchol for the treatment of liver diseases. OWL also granted us a right of first refusal, exercisable upon completion of our ARREST Study, to enter into a business transaction with OWL regarding the commercial exploitation of the data generated during the collaboration. In the future, we may seek additional collaborations of this nature.

- **In-license, develop or acquire additional drug candidates for the treatment of liver diseases**. Aramchol is directed at the treatment of liver diseases, particularly NASH, that have major global markets. Our intent is to explore opportunities to in-license, develop or acquire other molecules and/or conjugates for the treatment of liver diseases.

We believe that our strategy will increase the likelihood of advancing clinical development and potential commercialization of Aramchol in multiple indications, as well as increase awareness of liver disease and metabolic syndrome, our brand and our potential market share. In addition, through activating our pipeline expansion strategy we believe we could extrapolate additional commercial potential, as well as de-risk our company through reducing our reliance on the success of any one given trial or indication.

Unmet Need

Based on the limited treatment options, and the lack of approved therapy, for the treatment of NASH, we believe that there is a significant unmet need for a NASH-specific therapy. We believe that Aramchol has the potential to provide significant benefits in the treatment of this liver disease due to its ability to reduce liver fat in a dose dependent manner, lack of observable adverse side effects in our studies to date and ease of use through once-daily oral administration. Moreover, based in part on the Journal of Gastroenterology and Hepatology, we believe the increasing rates of diabetes and obesity worldwide likely means that a significant number of patients will be eligible for, and will be interested in, receiving a new therapy for the treatment of NASH if it becomes available on the market. We believe that Aramchol's observed positive metabolic effects, if confirmed in future studies, will position it as a valuable tool in the treatment of NASH in OD patients at an early stage of the disease, which can help to prevent both hepatic and cardiovascular complications.

Aramchol Formulation Development

There has been a progression of the formulations of Aramchol used so far in the preclinical and clinical studies. In the Phase IIA study, we administered a simple compressed tablet form that was developed directly from the suspension used in the Phase IA and IB studies and the preclinical studies in animals. Upon completion of our Phase IIA study, drug product formulation options were reviewed comprehensively, leading to the development of an

immediate-release tablet formulation for Aramchol.Based on this formulation, Aramchol tablets with matching placebos at 400 mg and 200 mg strengths have been developed to enable the convenient administration of 400 mg and 600 mg doses (for a 600 mg dose, patients will administer one 400 mg tablet and one 200 mg tablet). At the end of our Phase IIB study, we expect to determine the efficacious dose (400 mg or 600 mg). In case we select 600 mg, there may be an additional development of a single dose tablet of 600 mg.

Notwithstanding the foregoing, the optimized conventional tablet for the Aramchol free acid form may be suitable for Phase III clinical trial and commercial use, subject to minor alterations for dosage strength after confirmation of the efficacious dose. If we decide to develop the formulations of Aramchol salts due to the improvement in solubility and bioavailability and longer patent protection, we may conduct an appropriate bioequivalence study, or studies of the biological equivalence of two proprietary preparations of a drug, prior to administering an Aramchol salt formulation to patients in our clinical studies.

Potential Future Biomarkers for Non-Invasive Diagnosis of NAFLD and NASH

Currently, the initial diagnosis of NAFLD and/or NASH is based on elevated levels of liver enzymes, such as serum ALT levels, in blood tests. Once further evaluation excludes other reasons for liver disease, such as medications, viral hepatitis or excessive alcohol use, non-invasive imaging tests such as ultrasound, CT scans and MRS are good indicators of the presence of NAFLD and/or NASH. However, such tests are not reliable in assessing the degree of inflammation and fibrosis, which would distinguish between the diseases. Moreover, some of these tests generate high rates of false negatives; up to 20% in ultrasound and CT scans. Necro-inflammation, or premature cell death coupled with inflammation, hepatocellular ballooning, or a form of liver cell death, and the degree of fibrosis strongly predict the risk of disease progression, all are based on histology. Therefore, the liver biopsy is the gold standard approach for the diagnosis of inflammation and fibrosis associated with NASH and NAFLD, and the differentiation between them. However, the procedure-related morbidity, pain, sample errors and costs limit its use.

The current lack of specific, non-invasive diagnostic tools for patient monitoring and clinical drug development for NAFLD and NASH present a major challenge to the scientific and medical communities. Initiation of treatment depends on an accurate diagnosis of NASH, which for now can only be arrived at by biopsy, thus limiting patient care and prognosis. We believe that a non-invasive, reliable diagnostic tool is also needed for the assessment of the efficacy of treatment in a particular patient with NAFLD or NASH, once treatment is initiated.

In light of this unmet need, new non-invasive methods for the diagnosis of NASH have been developed or are currently under development. Among those, MRS is a validated, commonly used and non-invasive technique for in-vivo fat quantification. There is a growing position in the scientific and medical community to replace assessment of liver histology with MR-based imaging tests, as set forth in an article published in Gastroenterology in 2016 (150:7–10). This school of thought is one of foundations to maintain our strategy of utilizing MRS technology as an endpoint in our ARREST Study of Aramchol. If we are successful in our clinical trials in correlating fat reduction in the liver as measured by MRS with Aramchol's effect on inflammation in the liver, MRS may become a non-invasive biomarker with the ability to measure the effect of Aramchol in patients following treatment with the drug.

However, MRS does not measure inflammation, and thus the need for additional markers must still be addressed. As such, there is currently a growing interest in clinical prediction algorithms and biomarkers, such as the NAFLD fibrosis score, Enhanced Liver Fibrosis panel score and circulating biomarkers, such as CK-18, which is a marker of inflammation.

Recognizing this unmet need, we are collaborating with OWL, which developed the proprietary OWL LIVERTest®, a test seeking to stratify patients according to their metabolites profile. By correlating the findings of OWL LIVERTest® with liver biopsies in the patients enrolled in our studies, we are working towards finding a specific non-invasive test which would predict individual responses to Aramchol, which we believe could facilitate the market adoption of Aramchol. On July 8, 2015, we entered into a Research, Option and License Agreement and a Share

Purchase Agreement with respect to the foregoing. OWL. See “Item 4.B. Information on the Company—Business Overview—Strategic Collaborations, Research Arrangements and other Material Agreements—OWL.”

We hope that our efforts will lead to the identification of specific biomarkers, which will differentiate NASH from NAFLD patients without the need for liver biopsy, and serve as a tool for the prediction and assessment of Aramchol’s efficacy. The identification of such specific biomarkers would greatly improve Aramchol’s chances of qualifying for reimbursement from third-party payors, by providing an indication of the patients who are most likely to benefit from treatment with Aramchol.

Strategic Collaborations, Research Arrangements and other Material Agreements

OWL

On July 8, 2015, we entered into a Research, Option and License Agreement, or the OWL License Agreement with OWL, for the development of a non-invasive, blood-based complimentary diagnostic tool, which we believe could increase the likelihood of success of our Phase III trials and facilitate the market adoption of Aramchol. Pursuant to the terms of the OWL License Agreement, we will partially fund the research and development of the diagnostic tool in the amount of up to Euro 437,000 based on reaching development milestones. Subject to development under the OWL License Agreement, we have an option to exclusively license from OWL a complimentary diagnostic tool for NASH using Aramchol, or the OWL License Agreement Option, in consideration for the payment of a 10% royalty to OWL on an annual net sales of the complimentary diagnostic product. In addition, if OWL develops any other complimentary diagnostic tool for NASH not using Aramchol, it will pay us a royalty from revenues. Concurrently with the OWL License Agreement, we have entered into a Share Purchase Agreement, or the OWL SPA, pursuant to which we undertook to invest Euro 175,000 in OWL, subject to certain specified milestones. In addition, under the OWL SPA, OWL has granted us an option which will allow us to purchase additional shares up to 19.9% of OWL at the higher of the valuation as a then current round of financing or at a 15% premium on OWL's valuation in the most recent equity investments.

Upon exercise of the OWL License Agreement Option, we will own all rights, title and interest in and to (i) the complimentary diagnostic tool for NASH using Aramchol, excluding the OWL Markers (as defined in the OWL License Agreement) and any Licensed Technology (as defined in the OWL License Agreement) which are owned by OWL; (ii) the complimentary diagnostic tool for NASH using Aramchol intellectual property; and (iii) all Development Results (as defined in the OWL License Agreement).

University of California, San Diego

In February 2015, we entered into an Investigator Initiated Trial Agreement with the University of California, San Diego to conduct a Phase IIA Study for the treatment of HIV associated with Lipodystrophy and NAFLD, or the ARRIVE Study. The ARRIVE Study principal investigator is Dr. Rohit Loomba, a member of our scientific advisory board. The ARRIVE Study is a randomized, double-blinded, allocation-concealed, placebo-controlled, proof-of-concept Phase IIA clinical trial. The study will evaluate up to 50 patients with HIV-associated lipodystrophy and NAFLD, with either Aramchol at 600 mg or placebo for 16 weeks. Pre- and post-treatment MRI-measured liver fat content and total body fat via DEXA will be compared. The primary end point of successful therapy will be an improvement in hepatic steatosis as measured by MRI. Secondary endpoints will be an improvement in total body fat, metabolic profile, and liver biochemistry. On December 1, 2015 we announced that the FDA has cleared our IND application for the ARRIVE Study and on March 1, 2016, we announced that we have randomized the first patient in the ARRIVE study.

Perrigo API Ltd.

On January 28, 2015, the Company entered into a Manufacturing Services Agreement, or the Perrigo Agreement, with Perrigo API Ltd., or Perrigo, a subsidiary of Perrigo Company plc, for, among other things, the large-scale production of Aramchol API and the scale-up and manufacturing process optimization for large-scale production of the Aramchol API. To date, we have completed the process of transferring the development and scale-up process of the manufacturing process from Cambridge Major Laboratories to Perrigo. Pursuant to the Perrigo Agreement, Perrigo will provide manufacturing process, optimization services for large-scale production of the Aramchol API, manufacture the Aramchol API pursuant to current good manufacturing practices, or cGMP, and perform additional development services regarding scale-up and manufacturing optimization for the Aramchol API. In consideration for the services to be provided by Perrigo, the Company agreed to pay in accordance with the Perrigo Agreement a maximum aggregate amount of approximately $3.6 million U.S. dollars to Perrigo. The Perrigo Agreement also provides Perrigo, under certain circumstances, with the option to manufacture commercial supplies of the Aramchol API in the future. To date, Perrigo has manufactured 3 pilot batches of Aramchol. The material obtained is of appropriate quality and was produced under GMP. Additional development work pertaining to the scale-up and optimization of the process is currently being done by Perrigo. Based on the results of the optimization studies the parties to the Perrigo Agreement will decide whether they wish to complete all its stages.

Itamar Medical Ltd.

On September 29, 2014, we purchased 60 EndoPAT™ devices and accessories from, and entered into a collaboration with, Itamar to include an assessment of endothelial, or arterial, function in our ARREST Study of Aramchol in NASH patients who are obese and also suffer from insulin resistance. The purchase price for the EndoPAT™ devices and accessories was approximately $750,000.

Aventis Pharma Deutschland GmbH

In September 2002, we entered into an agreement, which we refer to as the Aventis Agreement, with Aventis, which merged with Sanofi S.A. and the company is now called Sanofi S.A., in connection with the settlement of court proceedings regarding an invention covered by Israeli patent application 123998 and PCT/IL99/00173. The invention relates to certain FABACs, pharmaceutical compositions containing FABACs and the use of FABACs for dissolving cholesterol gallstones in bile and preventing the formation thereof, as well as for the prevention and reduction of atherosclerosis, or the hardening of the arteries. Such court proceedings resulted from a claim filed by us and Prof. Tuvia Gilat, our founder, in the Tel- Aviv District Court seeking a declaratory judgment that Prof. Gilat was the sole inventor of the invention and the owner of all rights in and to the invention and the patent application with respect thereto, and that neither Aventis nor anyone on its behalf has any rights in or to the invention or such patent application. We filed the claim with Prof. Gilat based on assertions by Aventis that it had certain rights to the invention as a result of the participation of one of its employees in the discovery of the same. Under the Aventis Agreement, Aventis agreed that we had the exclusive worldwide right to commercialize the invention and we agreed to pay Aventis a royalty of 10% in respect of all income that we or our affiliates may receive from the commercialization of such invention for the prevention and treatment of cholesterol gallstones (less certain standard deductions, including taxes, credits, allowances, rebates, freight and insurance costs), for as long as there is a valid patent or pending patent application covering such invention. Once all valid patents covering the invention expire, which will occur in 2018, and provided that one of Aventis' other patents that covers an aspect of the invention is still valid and has received marketing approval prior to the expiration of all the patents covering the invention, the royalty will be reduced to 5%.

The Aventis Agreement does not contain any diligence obligations that require us to exert any special efforts to develop a product for the prevention and treatment of cholesterol gallstones, nor are we contractually required to meet any milestones in respect of the development or commercialization of the invention. We have not yet paid, nor do we currently owe, any amounts to Aventis under the Aventis Agreement. Additionally, after experiencing poor patient recruitment and due to higher-priority clinical programs, at this point in time we have decided not to pursue the indications of cholesterol gallstones and we believe that it is unlikely that we will revive another study in cholesterol gallstones.

Unipharm

On October 7, 2000, in connection with a certain share subscription agreement, we sent a letter to Unipharm Ltd., or Unipharm, pursuant to which we agreed to negotiate the grant of an exclusive license to Unipharm with respect to the use of patents within our first patent family covering the composition of matter of Aramchol within Israel on to-be-agreed upon terms and conditions. The letter stated that, if granted, such license would at all times be subject to our best interests, as determined in our sole discretion, and all approvals and proceedings required by agreement or by law. As of the date hereof, no such definitive agreement has been executed with regard to this matter and at this stage we have no intention to pursue such an agreement. The letter is silent as to term, termination and whether or not it is binding.

Competition

The pharmaceutical industry is characterized by rapidly evolving technology, intense competition and a highly risky, costly and lengthy research and development process. Adequate protection of intellectual property, successful product development, adequate funding and retention of skilled, experienced and professional personnel are among the many factors critical to success in the pharmaceutical industry.

We believe that Aramchol offers key potential advantages over other drugs in development that could enable Aramchol, if approved for these indications, to capture meaningful market share. We believe that Aramchol's ability, as observed in our studies to date, to reduce liver fat content without adverse side effects, which we believe may prove to have an anti-inflammatory effect, and convenient once-daily oral administration make Aramchol a potentially valuable drug for the treatment of liver disease.

Other companies, including Intercept Pharmaceuticals, Inc. and Genfit S.A., have molecules currently in Phase III clinical development, and Gilead Sciences, Inc., Tobira Therapeutics Inc., Conatus pharmaceuticals Inc., Novo Nordisk and Immuron have molecules and/or antibodies in Phase IIB clinical development for the treatment of NASH and the fibrosis associated therewith. Antibodies cannot be delivered orally. There are a host of other potential competitors in earlier stages of development relative to us for the treatment of NASH including, but not limited to Galectin therapeutics Inc., Arisaph pharmaceuticals Inc, AstraZeneca, Bristol-Myers Squibb, Medicinova and Nimbus. Some of these companies are focusing their trials on NASH patients with advanced fibrosis, whereas our studies relate to NASH, or the onset of fat accumulation in and inflammation of the liver, in which we expect that Aramchol will reduce and eventually eliminate liver inflammation by reducing the fat content of the liver.

We believe that the characteristics of Aramchol, as exhibited in our clinical studies to date, including its convenient once-daily oral administration and lack of observable adverse side effects, position it well against the potential competition in the NASH market. Currently used treatments are not approved by applicable regulatory authorities for the indication they are prescribed or used for as they have not proven efficacious in well-designed clinical studies. In addition, drugs in development for the treatment of NASH may, according to published data, be injectable or require intravenous delivery and may cause side effects, such as dyslipidemia, or an abnormal amount of lipids in the blood, severe itching, which can be highly inconvenient for patients with chronic diseases, such as NASH, and which may result in low patient compliance.

Notwithstanding the foregoing, see “Item 3. Key Information—Risk Factors—Risks Related to Our Business, Industry and Regulatory Requirements—Our market is subject to intense competition. If we are unable to compete effectively, Aramchol or any other product candidate that we develop may be rendered noncompetitive or obsolete.”

Intellectual Property and Patent Strategy

The proprietary nature of, and protection for, our product candidates and our discovery programs for new indications, processes and know-how are important to our business. We own patent rights to Aramchol in various jurisdictions worldwide, including within and outside of Israel. We have sought patent protection in the United States and internationally for Aramchol and our discovery programs, and any other inventions to which we have rights, where available and when appropriate. We expect that patent protection covering the use of Aramchol for the treatment of fatty liver will not expire until 2022 (2021 in Israel), subject to any applicable extensions then-available. Within Israel, we agreed to negotiate the grant of an exclusive license to Unipharm Ltd. , or Unipharm, with respect to the use of patents within our first patent family covering the composition of matter of Aramchol on to-be-agreed upon terms and conditions. We are not in negotiations with Unipharm and no definitive agreement has been executed as of the date hereof.

Our policy is to pursue, maintain and defend patent rights, whether developed internally or licensed from third parties, and to protect the technology, inventions and improvements that are commercially important to the development of

our business. We also rely on trade secrets that may be important to the development of our business.

Patent Portfolio for Aramchol (First-in-Class Synthetic FABAC)

The patent portfolio for Aramchol contains patents and pending patent applications directed to composition of matter, manufacturing methods and methods of use. As of March 10, 2016, we own six U.S. patents, and corresponding foreign patents and pending patent applications, as detailed below. We have also recently filed a PCT patent application for second generation FABAC compounds.

The first patent family discloses and claims FABACs, including Aramchol, as well as methods for preventing or dissolving cholesterol gallstones in bile and reducing or preventing arteriosclerosis using FABACs. This patent family includes three issued U.S. patents and an issued European patent that was validated in Austria, Belgium, Cyprus, Denmark, Finland, France, Germany Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Monaco, Netherlands, Portugal, Romania, Slovenia, Spain, Sweden, Switzerland and the United Kingdom. Corresponding patents have been granted in Australia, Brazil, Canada, China, Czech Republic, Eurasia, Hungary, Indonesia, Israel, Japan, Korea, Mexico, New Zealand, Norway, Poland, Turkey and the Ukraine. If the appropriate maintenance, renewal, annuity or other governmental fees are paid, the non-extended patent term for this patent family is due to expire on March 25, 2019, with the exception of the Israeli patent, which is due to expire on April 8, 2018.

The second patent family discloses and claims additional FABACs with different conjugation moieties, as well as the use of these and the compounds disclosed in the first patent family above, including Aramchol, in the treatment of fatty liver, reduction of serum cholesterol and treatment of hyperglycemia and diabetes. This patent family includes a U.S. patent directed to the treatment of fatty liver a U.S. patent directed to reduction of serum cholesterol by administering additional forms of FABACs, and a U.S. patent (Continuation-in-Part) directed to the treatment of hyperglycemia and diabetes. This patent family also includes two European patents, one patent which was validated in Austria, Belgium, Cyprus, Denmark, Finland, France, Germany Ireland, Italy, Luxembourg, Monaco, Netherlands, Portugal, Spain, Sweden, Switzerland, Turkey and the United Kingdom, and the second patent which was validated in Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Netherlands, Spain, Sweden, Switzerland, Turkey and the United Kingdom. The family also includes patents in Australia, Canada, China, Czech Republic, Eurasia, Indonesia, Japan, Korea, Israel, Mexico, New Zealand, Norway, Poland and the Ukraine. Foreign patent applications are pending in Hungary and the Czech Republic. If the appropriate maintenance, renewal, annuity or other governmental fees are paid, the non-extended patent term for this patent family is due to expire on April 15, 2022, with the exception of the Israeli patent, which is due to expire on April 17, 2021. The terms of the U.S. patents in this family have been extended due to patent term adjustments of 567 days for U.S. Patent 7,501,403, which is directed to the treatment of fatty liver, and 24 days for U.S. Patent 8,110,564, which is directed to reduction of serum cholesterol, and 356 days for U.S. Patent 8,975,246, which is directed to disorders associated with altered glucose metabolism or insulin action.

A third patent family that is due to expire on February 1, 2030, discloses the use of FABACs in the treatment, prevention and inhibition of progression of Alzheimer’s Disease, cerebral amyloid angiopathy and other brain diseases characterized by amyloid plaque deposits. This patent family includes an issued European patent that was validated in France, Germany, Switzerland and the United Kingdom.

A fourth patent family, including one PCT patent application, discloses and claims second generation FABAC compounds.

A fifth patent family, including one PCT patent application, covers the use of Aramchol for the treatment of lipodystrophy.

A sixth patent family, including one provisional patent application, discloses and claims compositions comprising second generation FABAC compounds.

The seventh and an eighth patent families, each including one Israeli patent application, cover additional therapeutic uses of Aramchol.

It is possible that the term of the patents issued in the United States within our first patent family, which includes the composition of matter patents, may be extended up to five additional years under the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. Patent term extension or supplementary protection certificates may be available in certain foreign countries upon regulatory approval. Independent of patent term extensions, five years of data exclusivity may be provided for this patent in the United States automatically from the day of receiving FDA approval of an NCE in the United States. If the Company pursues commercialization of Aramchol in other jurisdictions, longer periods of data exclusivity may pertain.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future product candidates and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We believe that our patents provide broad and comprehensive coverage for the use of Aramchol for the treatment of certain liver diseases. However, the patent positions of biopharmaceutical companies, such as ourselves, are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for the technology will depend on our success in obtaining effective claims and enforcing those claims once granted. There is no certainty that any of the Company’s pending patent applications will result in the issuance of any patents. The issued patents and those that may be issued in the future, may be challenged, narrowed, circumvented or found to be invalid or unenforceable, which could limit our ability to stop competitors from marketing related products or the length of term of patent protection that we may have for our products. In addition, our competitors may independently develop similar technologies or duplicate any technology developed by us, and the rights granted under any issued or future patents may not provide us with any meaningful competitive advantages against these competitors. Furthermore, because of the extensive time required for development, testing and regulatory review of a potential product, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of such patent. For more risks associated with the protection of our licensed intellectual property, see “Item 3. Key Information—Risk Factors—Risks Related to Our Intellectual Property.”

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our proprietary information. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, such agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors or others.

Seasonality

Our business and operations are generally not affected by seasonal fluctuations or factors.

Raw Materials and Suppliers

We believe that the raw materials that we require to manufacture Aramchol are readily available commodities commonly used in the pharmaceutical industry. Demand for certain of the required raw materials, such as cholic acid, has recently increased, resulting in a price increase. We anticipate that the price levels of cholic acid will revert back to prior levels and will not experience continued volatility as a result of the entrance of additional manufacturers into the cholic acid market.

Manufacturing

We do not own or operate manufacturing facilities for the production of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials, API and finished product for our preclinical research and clinical trials, including our ARREST Study for Aramchol for the treatment of NASH. We do not have long -term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of our product candidate if it is approved; however, the Perrigo Agreement (as described herein) provides Perrigo with the option to negotiate an exclusive commercial contract for the manufacture of commercial supplies of the Aramchol API in the future for a minimum term of five years. If our product candidate or future

product candidates are approved by any regulatory agency, we intend to enter into agreements with a third-party contract manufacturer and one or more back-up manufacturers for the commercial production of those products. Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval. We currently employ internal resources to manage our manufacturing contractors. The relevant manufacturers of our drug products for our current preclinical and clinical trials have advised us that they are compliant with both cGMP and current Good Laboratory Practices, or cGLP.

There can be no assurance that our product candidate, if approved, can be manufactured in sufficient commercial quantities, in compliance with regulatory requirements and at an acceptable cost. We and our contract manufacturers are, and will be, subject to extensive governmental regulation in connection with the manufacture of any pharmaceutical products or medical devices. We and our contract manufacturers must ensure that all of the processes, methods and equipment are compliant with cGMP and cGLP for drugs on an ongoing basis, as mandated by the FDA and other regulatory authorities, and conduct extensive audits of vendors, contract laboratories and suppliers.

We currently engage the services of Cambridge Major Laboratories, a leading provider of chemistry services to the global pharmaceutical industry, to develop and manufacture Aramchol clinical API. However, on January 28, 2015, we entered into the Perrigo Agreement with Perrigo, a subsidiary of Perrigo Company plc, for, among other things, the large-scale production of Aramchol's API and the scale-up and manufacturing process optimization for large-scale production of the Aramchol API. As such, the Company is currently in the process of transferring the development and scale-up of the manufacturing process from Cambridge Major Laboratories to Perrigo. See "Item 4.B. Information on the Company—Business Overview—Strategic Collaborations, Research Arrangements and other Material Agreements—Perrigo API Ltd." for a more information regarding the Perrigo Agreement.

Contract Research Organizations

We outsource certain clinical trial activities to CROs. Our clinical CROs comply with guidelines from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, which attempt to harmonize the FDA, the EMA, and the Pharmaceuticals and Medical Devices Agency of Japan regulations and guidelines. We create and implement the drug development plans and manage the CROs according to the specific requirements of the drug candidate under development. To the extent clinical research is overseen by the CROs (or us in the future), compliance with certain federal regulations, including but not limited to 21 C.F.R. parts 50, 54, 56, 58 and 312, which pertain to, among other things, IRBs, informed consent, financial conflicts of interest by investigators, correct administration of treatment, follow up of adverse events, good laboratory practices and submitting IND applications, may be required.

Marketing, Sales and Commercialization

Given our stage of development, we do not have any internal sales, marketing or distribution infrastructure or capabilities. In the event we receive regulatory approval for Aramchol, we intend, where appropriate, to pursue commercialization relationships, including strategic alliances and licensing, with pharmaceutical companies and other strategic partners, which are equipped to market and/or sell our products, if any, through their well-developed sales, marketing and distribution organizations in order to gain access to global markets. In addition, we may out-license some or all of our worldwide patent rights to more than one party to achieve the fullest development, marketing and distribution of any products we develop. Over the longer term, we may consider ultimately building an internal marketing, sales and commercial infrastructure.

Environmental Matters

We, our agents and our service providers, including our manufacturers, may be subject to various environmental, health and safety laws and regulations, including those governing air emissions, water and wastewater discharges,

noise emissions, the use, management and disposal of hazardous, radioactive and biological materials and wastes and the cleanup of contaminated sites. We believe that our business, operations and facilities, including, to our knowledge, those of our agents and service providers, are being operated in compliance in all material respects with applicable environmental and health and safety laws and regulations. All information with respect to any chemical substance is filed and stored as a Material Safety Data Sheet, as required by applicable environmental regulations. Based on information currently available to us, we do not expect environmental costs and contingencies to have a material adverse effect on us. However, significant expenditures could be required in the future if we, our agents or our service providers are required to comply with new or more stringent environmental or health and safety laws, regulations or requirements.

Government Regulation and Product Approval

Governmental authorities in the United States and in other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing and export and import of products such as those we are developing. Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States and by the Committee on Human Medicinal Products, or CHMP, via the EMA and European Commission through the MAA process before they may be legally marketed in Europe. Our product candidate and future product candidates will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

We are conducting a global development program for Aramchol for the treatment of NASH in patients who are obese and also suffer from insulin resistance, and we may make our submissions for regulatory approval in parallel; initially in Europe and in the United States. Typically, approval time in the United States with the FDA for an NDA is faster than that within Europe with the EMA and the European Commission for an MMA, especially when the novelty of the submission is considered. First in class, high medical need and rare disease drugs can experience faster review. Nevertheless, marketing and pricing approval presents a further delay in many countries that should be considered in addition to the regulatory approvals noted above.

United States Government Regulation

NDA Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and implementing regulations and guidance documents. Failure to comply with the applicable U.S. requirements at any time during the product development process or approval process, or after approval, may subject an applicant to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, warning letters, product seizures, total or partial suspension of production or distribution, or injunctions, fines, disgorgement, and civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices, or GLPs, or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCPs, to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA;
-

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMPs to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

- satisfactory completion of FDA inspections of clinical sites and GLP toxicology studies; and

- FDA review and approval of the NDA.

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

Once a product candidate is identified for development, it enters the preclinical or nonclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical testing may continue after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will also include a clinical trial protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND, due to safety concerns or non-compliance, and may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs and relevant FDA regulations. These regulations include the requirement that all research subjects provide informed consent. Further, an IRB must review and approve the plan for any clinical trial, including the informed consent document, before it commences at any institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative and must monitor the study until completed. All clinical trials must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject inclusion and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors must also report within set timeframes to FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure, or any findings from other studies or animal or in-vitro testing that suggest a significant risk in humans exposed to the drug.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase I*. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- *Phase II*. Clinical trials are performed on a limited patient population intended to identify possible adverse effects and risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase III*. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. Phase III clinical trials are conducted to provide sufficient data for the statistically valid evidence of safety and efficacy.

Human clinical trials are inherently uncertain and Phase I, Phase II and Phase III testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points are typically prior to the submission of an IND, at the end of Phase II and before an NDA is submitted. Meetings at other times may also be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development.

Sponsors typically use the meeting at the end of Phase II to discuss their Phase II clinical results and present their plans for the pivotal Phase III clinical trial that they believe will support the approval of the NDA. If a Phase II clinical trial is the subject of discussion at the end of Phase II meeting with the FDA, a sponsor may be able to request a Special Protocol Assessment, or SPA, the purpose of which is to reach agreement with the FDA on the Phase III clinical trial protocol design and analysis that will form the primary basis of an efficacy claim.

According to published guidance on the SPA process, a sponsor which meets the prerequisites may make a specific request for an SPA and provide information regarding the design and size of the proposed clinical trial. The FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and that evaluation may result in discussions and a request for additional information. An SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the record. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began. There is no indication that we will be able to meet the requirements necessary for an SPA.

Concurrent with clinical trials, sponsors usually complete any remaining animal safety studies and also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing commercial quantities of the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug and the manufacturer must develop methods for testing the quality, purity and potency of the drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its proposed shelf-life.

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. We will seek a waiver of these fees as a small company submitting its first marketing application. If the waiver is granted it would not extend to establishment or product fees. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Submission of a pediatric assessment is not required for an application to market a product for an orphan-designated indication, and waivers are not needed at this time. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non- orphan indication(s).

Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA

reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured and tested. The FDA will also inspect selected clinical sites that participated in the clinical studies and may inspect the testing facilities that performed the GLP toxicology studies cited in the NDA.

Expedited Review and Approval

NDAs receive either standard or expedited review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive expedited review. The FDA has various specific programs, including Fast Track, Breakthrough Therapy, Priority Review, and Accelerated Approval, which, in different ways, are each intended to expedite the process for reviewing and approving drugs. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious or life-threatening diseases or conditions and fill unmet medical needs, and Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s). Priority review is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months. Although Fast Track, Breakthrough Therapy designation and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track or Breakthrough Therapy designated drug and expedite review of the application for a drug designated for priority review. The FDA will also provide Breakthrough Therapy designated drugs intensive guidance on an efficient drug development program and provide these drug developers with an organizational commitment from the FDA involving senior managers. Since sponsors can design clinical trials in a number of ways, in providing its guidance for drugs designated as breakthrough therapies, the FDA will seek to ensure that the sponsor of the product designated as a breakthrough therapy receives timely advice and interactive communications in order to help the sponsor design and conduct a development program as efficiently as possible. During these interactions, the FDA may suggest, or a sponsor can propose, alternative clinical trial designs (e.g., adaptive designs, an enrichment strategy, use of historical controls) that may result in smaller trials or more efficient trials that require less time to complete. Such trial designs could also help minimize the number of patients exposed to a potentially less efficacious treatment (i.e., the control group treated with available therapy).

Accelerated Approval, which is described in 21 C.F.R. § 314.500 *et seq*., provides for approval of a new drug that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. To be used in accelerated approval, a surrogate endpoint must be “reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence to predict benefit” on irreversible morbidity or mortality.” The term “reasonable likely” implies that some uncertainty remains about the relationship of the surrogate to the clinical benefit to the patient. Therefore, accelerated approval is typically contingent on a sponsor’s agreement to conduct additional post-approval studies to verify and describe the drug’s clinical benefit. Accelerated Approval does not change the standards for approval, but by allowing a demonstration of efficacy based on a surrogate endpoint may expedite the approval process.

Liver histology currently offers the best short-term method for tracking the progression of NASH. Certain features on histopathology provide some prognostic information regarding risk for progression. Steatohepatitis, not isolated fatty

liver, is associated with a substantial increase in the long-term risk of developing cirrhosis and liver-related outcomes (15, 35). This is believed to be related to the underlying inflammation and activation of pro-fibrogenic pathways in NASH. Based on this current understanding of the pathogenesis of NASH, one would expect that reversal of steatohepatitis would reduce the risk of developing cirrhosis. However, steatosis and inflammation can decrease as fibrosis advances (37). Therefore, the reversal of steatohepatitis with no evidence of progression to advanced fibrosis (stage 3 or 4), may be an acceptable surrogate endpoint suitable both for phase IIB and III trials that enroll patients with NASH and evidence of early fibrosis.

On September 23, 2014, the FDA granted Fast Track designation status to Aramchol for the treatment of OD patients with NASH.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our product candidates, U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for extension must be made prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five year and three year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Post-approval Requirements

Once an approval is granted, the FDA, European authorities and other regulatory authorities may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further regulatory authority review and approval. Some of these modifications, especially adding indications, would likely require additional clinical studies. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Any drug product manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things record-keeping requirements; good manufacturing practices; reporting of adverse experiences with the drug; providing the FDA with updated safety and efficacy information; drug sampling and distribution requirements; notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and complying with FDA promotion and advertising requirements.

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Reimbursement

Sales of our products will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Modernization Act imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries under Part B. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Parts A and B, Part D reimbursement is not set by the government, but rather by private insurers. Moreover, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Recently, the Centers for Medicare & Medicaid Services proposed a rule that would enable Part D plans to offer fewer drugs than would otherwise be the case. The impact of this proposed rule on a product such as ours cannot be predicted at this time, but it could have a material adverse impact on our product were it being marketed at this time. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the Modernization Act may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor’s product could adversely affect the sales of our product candidates. If

third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Affordable Care Act, enacted in March 2010, is expected to have a significant impact on the health care industry. The Affordable Care Act is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the Affordable Care Act is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the impact of the Affordable Care Act on pharmaceutical companies. See “Item 3. Key Information—Risk Factors—Risks Related to Our Business, Industry and Regulatory Requirements—We expect the healthcare industry to face increased limitations on reimbursement, rebates and other payments as a result of healthcare reform, which could adversely affect third-party coverage of our products and how much or under what circumstances healthcare providers will prescribe or administer our products.”

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally tend to be significantly lower.

Anti-Kickback and False Claims Laws

In the United States, the research, manufacturing, distribution, sale and promotion of drug products and medical devices are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice, state Attorneys General, and other state and local government agencies. For example, sales, marketing and scientific/educational grant programs must comply with the Medicare-Medicaid Anti-Fraud and Abuse Act, as amended (the "Anti-Kickback Statute"), the False Claims Act, as amended, the privacy regulations promulgated under the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

In the United States, we are subject to complex laws and regulations pertaining to healthcare "fraud and abuse," including, but not limited to, the Anti-Kickback Statute, the federal False Claims Act, and other state and federal laws and regulations. The Anti- Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid.

The federal False Claims Act prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services.

There are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. In addition, a similar federal requirement requires manufacturers to track and report to the federal government certain payments made to physicians and teaching hospitals made in the previous calendar year. These laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state and federal authorities.

European Economic Area

In addition to approval in the United States, we currently intend to seek regulatory approval of Aramchol in the EU. As such, a summary of the EU regulatory processes follows below.

A medicinal product may only be placed on the market in the European Economic Area, or EEA, composed of the 28 EU member states, plus Norway, Iceland and Lichtenstein, when a marketing authorization has been issued by the competent authority of a member state pursuant to Directive 2001/83/EC (as recently amended by Directive 2004/27/EC), or an authorization has been granted under the centralized procedure in accordance with Regulation (EC) No. 726/2004 or its predecessor, Regulation 2309/93. There are essentially three community procedures created under prevailing European pharmaceutical legislation that, if successfully completed, allow an applicant to place a medicinal product on the market in the EEA.

Centralized Procedure

Regulation 726/2004/EC now governs the centralized procedure when a marketing authorization is granted by the European Commission, acting in its capacity as the European Licensing Authority on the advice of the EMA. That authorization is valid throughout the entire community and directly or (as to Norway, Iceland and Liechtenstein) indirectly allows the applicant to place the product on the market in all member states of the EEA. The EMA is the administrative body responsible for coordinating the existing scientific resources available in the member states for evaluation, supervision and pharmacovigilance of medicinal products. Certain medicinal products, as described in the Annex to Regulation 726/2004, must be authorized centrally. These are products that are developed by means of a biotechnological process in accordance with Paragraph 1 to the Annex to the Regulation. Medicinal products for human use containing a new active substance for which the therapeutic indication is the treatment of acquired immune deficiency syndrome, or AIDS, cancer, neurodegenerative disorder or diabetes must also be authorized centrally. Starting on May 20, 2008, the mandatory centralized procedure was extended to autoimmune diseases and other immune dysfunctions and viral diseases. Finally, all medicinal products that are designated as orphan medicinal products pursuant to Regulation 141/2000 must be authorized under the centralized procedure. An applicant may also opt for assessment through the centralized procedure if it can show that the medicinal product constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorization centrally is in the interests of patients at the community level. For each application submitted to the EMA for scientific assessment, the EMA is required to ensure that the opinion of the Committee for Medicinal Products for Human Use, or CHMP, is given within 210 days after receipt of a valid application. This 210 days period does not include the time that the applicant to answer any questions raised during the application procedure, the so-called ‘clock stop’ period. If the opinion is positive, the EMA is required to send the opinion to the European Commission, which is responsible for preparing the draft decision granting a marketing authorization. This draft decision may differ from the CHMP opinion, stating reasons for diverging for the CHMP opinion. The draft decision is sent to the applicant and the member states, after which the European Commission takes a final decision. If the initial opinion of the CHMP is negative, the applicant is afforded an opportunity to seek a re-examination of the opinion. The CHMP is required to re-examine its opinion within 60 days following receipt of the request by the applicant. All CHMP refusals and the reasons for refusal are made public on the EMA website. Without a centralized marketing authorization it is prohibited to place a medicinal product that must be authorized centrally on the market in the EU.

Mutual Recognition and Decentralized Procedures

With the exception of products that are authorized centrally, the competent authorities of the member states are responsible for granting marketing authorizations for medicinal products placed on their national markets. If the applicant for a marketing authorization intends to market the same medicinal product in more than one member state, the applicant may seek an authorization progressively in the community under the mutual recognition or decentralized procedure. Mutual recognition is used if the medicinal product has already been authorized in a member state. In this case, the holder of this marketing authorization requests the member state where the authorization has been granted to act as reference member state by preparing an updated assessment report that is then used to facilitate mutual recognition of the existing authorization in the other member states in which approval is sought (the so-called concerned member state(s)). The reference member state must prepare an updated assessment report within 90 days of receipt of a valid application. This report together with the approved Summary of Product Characteristics, or SmPC

(which sets out the conditions of use of the product), and a labeling and package leaflet are sent to the concerned member states for their consideration. The concerned member states are required to approve the assessment report, the SmPC and the labeling and package leaflet within 90 days of receipt of these documents. The total procedural time is 180 days.

The decentralized procedure is used in cases where the medicinal product has not received a marketing authorization in the EU at the time of application. The applicant requests a member state of its choice to act as reference member state to prepare an assessment report that is then used to facilitate agreement with the concerned member states and the grant of a national marketing authorization in all of these member states. In this procedure, the reference member state must prepare, for consid