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The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PROSPECTUS SUPPLEMENT (Subject to Completion) Dated February 1, 2017
(To Prospectus dated November 25, 2014)

Shares

Common Stock

We are offering shares of our common stock. Our common stock is listed for trading on The NASDAQ Capital Market under the symbol "CBAY." On January 31, 2017, the last reported sale price of our common stock on the NASDAQ Capital Market was $1.86 per share.

The aggregate market value of our outstanding common equity held by non-affiliates as of January 31, 2017, was approximately $51.8 million, based on 23,571,103 shares of outstanding common stock, of which 21,593,917 shares were held by non-affiliates, and a per share price of $2.40, the closing price on January 5, 2017. As of the date of this prospectus supplement, we have offered and sold 124,100 shares of our common stock for $308,202 pursuant to General Instruction I.B.6. of Form S-3 during the 12 calendar month period that ends on, and includes, the date of this prospectus supplement.

Investing in our securities involves significant risks. See " Risk Factors" beginning on page S-5 of this prospectus supplement and on page 5 of the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	*Total*
Public offering price	**$**	**$**
Underwriting discounts and commissions (1)	**$**	**$**
Proceeds, before expenses, to CymaBay	**$**	**$**

(1) We have also agreed to reimburse the underwriters for fees and expenses incurred by them in connection with this offering. See "Underwriting" beginning on page S-5 of this prospectus supplement for more information regarding underwriting discounts and commissions and expense reimbursement.

The underwriters may also purchase up to an additional shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement.

The underwriters expect to deliver the shares against payment in New York, New York on , 2017.

Sole Book Running Manager

JonesTrading

Lead Manager

LifeSci Capital LLC

, 2017

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PROSPECTUS SUPPLEMENT

PROSPECTUS

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated November 25, 2014, including the documents incorporated by reference therein, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in the accompanying prospectus — the statement in the document having the later date modifies or supersedes the earlier statement.

Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell shares pursuant to this prospectus supplement with a value of more than one-third of our public float as set forth on the cover page of this prospectus supplement less the $308,202 of shares sold pursuant to General Instruction I.B.6. of Form S-3 during the 12 calendar month period that ends on, and includes, the date of this prospectus supplement (approximately $17.0 million).

We have suspended, and during the duration of the offering to which this prospectus supplement relates we are no longer offering, any securities pursuant to the prospectus supplement relating to the offer and sale of shares pursuant to the Controlled Equity Offering℠ sales agreement with Cantor Fitzgerald & Co. filed with the Securities and Exchange Commission on December 30, 2016.

We have not, and the underwriters have not, authorized anyone to provide you with information different from that contained in or incorporated by reference into this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You also should read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement titled “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference.”

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

This prospectus supplement and the accompanying prospectus contain summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus is a part, and you may obtain copies of those documents as described below under the section titled "Where You Can Find Additional Information."

This prospectus supplement and the accompanying prospectus contain and incorporate by reference market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus supplement and the accompanying prospectus and the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading "Risk Factors" contained in this prospectus supplement and the accompanying prospectus and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement and the accompanying prospectus. Accordingly, investors should not place undue reliance on this information.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus supplement and the accompanying prospectus to "CymaBay" the "Company," the "Registrant," "us," "we" and "our" are to CymaBay Therapeutics, Inc., a Delaware corporation.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information appearing elsewhere or incorporated by reference into this prospectus supplement and the accompanying prospectus and may not contain all of the information that is important to you. You should read this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including "Risk Factors" beginning on page S-5 in this prospectus supplement and incorporated by reference from our most recent Annual Report on Form 10-K and most recent Quarterly Report on Form 10-Q, before making an investment decision.

Company Overview

We are a clinical-stage biopharmaceutical company focused on developing therapies to treat specialty and orphan diseases with high unmet medical need. We are currently developing seladelpar (MBX-8025) for the treatment of various orphan liver and lipid diseases. In May 2016, we announced results from a Phase 2 clinical study of seladelpar in patients with primary biliary cholangitis (PBC). The study was intended to enroll approximately 75 patients with PBC who had an inadequate response to ursodiol and randomize them to receive either placebo or seladelpar (either 50 mg or 200 mg) once-daily for 12 weeks. Despite the occurrence of three cases of asymptomatic, reversible transaminase elevations (two in the 200 mg and one in the 50 mg cohorts), data from 35 patients evaluated for efficacy demonstrated that treatment with seladelpar resulted in statistically significant reductions in the primary endpoint of alkaline phosphatase (ALP). The mean decreases from baseline in ALP for the 50 and 200 mg dose groups were 53% and 63%, respectively, vs. 2% for placebo ($p < 0.0001$ for both). We made the decision to discontinue the study early after review of safety and efficacy data demonstrated clear proof-of-concept and need for further dose reduction to optimize clinical safety and efficacy. In December 2016, we initiated a dose-ranging Phase 2 trial of seladelpar at lower doses in patients with PBC. In October 2016, seladelpar received European Medicines Agency (EMA) PRIority MEdicines (PRIME) designation for the treatment of PBC. In March 2016, we announced data from a second Phase 2 clinical study evaluating seladelpar in 13 patients with homozygous familial hypercholesterolemia (HoFH). Five patients in this study experienced what we believe was a clinically meaningful maximal decrease in low density lipoprotein (LDL-C) of greater than 20% with three of them having decreases greater than 30%. However, given the variability in responses observed in this study, including a number of patients that did not experience a decrease in LDL-C, we believe additional proof-of-concept data would be warranted before determining whether or not to advance to a registration study of seladelpar in patients with HoFH. We also believe that seladelpar could have utility in the treatment of severe hypertriglyceridemia (SHTG) and the more prevalent, but high unmet need, indication of nonalcoholic steatohepatitis (NASH). We have obtained orphan-drug designations for seladelpar in PBC, HoFH and SHTG (Frederickson type I or V hyperlipoproteinemia).

Arhalofenate, is being developed for the treatment of gout. Arhalofenate has been studied in five Phase 2 clinical trials in patients with gout and consistently demonstrated the ability to reduce gout flares and reduce serum uric acid (sUA). Gout flares are recurring and painful episodes of joint inflammation that are triggered by the presence of monosodium urate crystals that form as a result of elevated sUA levels. We believe the potential for arhalofenate to prevent or reduce flares while also lowering sUA could differentiate it from currently available treatments for gout and classify it as the first potential drug in what we believe could be a new class of gout therapy referred to as Urate Lowering Anti-Flare Therapy (ULAFT). Arhalofenate has established a favorable safety profile in clinical trials involving over 1,100 patients exposed to date. We have completed end of Phase 2 discussions with the FDA and scientific advice discussions with the EMA. In January 2017, we announced we had entered into an exclusive licensing agreement with Kowa Pharmaceuticals America, Inc. for the development and commercialization of arhalofenate in the U.S. (including all possessions and territories). Under the terms of the agreement, we have received an up-front payment of $5 million, and will receive potential milestone payments of up to $10 million based on the initiation of specific development activities, and are

eligible to receive up to an additional $190 million in payments based upon the achievement of specific development, regulatory and sales milestones. We are also eligible to receive tiered, double digit royalties on future sales of arhalofenate products. Kowa will be responsible for all development and commercialization costs. We retain full development and commercialization rights for the rest of the world and intend to partner arhalofenate in geographies outside the U.S. and its possessions and territories.

CymaBay Strategy

Our goal is to become a leading biopharmaceutical company focused on developing and commercializing proprietary new medicines for specialty and orphan diseases with high unmet medical need. Key elements of our strategy are to:

- develop seladelpar for patients with primary biliary cholangitis (PBC);
- develop seladelpar for other high unmet need or orphan indications focused on lipid and liver diseases;
- partner with third-parties for the development and commercialization of arhalofenate outside the U.S. for patients with gout; and
- strengthen our patent portfolio and other means of protecting exclusivity.

Risks Associated with our Business

Our business is subject to numerous risks. You should read these risks before you invest in our common stock. In particular, our risks include, but are not limited to, the following:

- We will need additional capital in the future to sufficiently fund our operations and research;
- We depend on the success of our product candidates, seladelpar and arhalofenate, which are still under clinical development and we may not obtain regulatory approval or successfully commercialize either of these product candidates;
- We depend on the successful completion of clinical trials for our product candidates, including seladelpar and arhalofenate, and the positive clinical results obtained for our product candidates in prior clinical studies may not be repeated in future clinical studies;
- We have only recently commenced testing of seladelpar in clinical studies for the indications which we are currently pursuing for seladelpar, including homozygous familial hypercholesterolemia (HoFH) and Primary Biliary Cholangitis (PBC). If seladelpar does not demonstrate safety or efficacy in the treatment of any of these indications, or if the benefits of treatment with seladelpar do not outweigh the risks, our ability to successfully develop and commercialize seladelpar may be adversely affected;
- Our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance;
- Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales; and
- If any product candidate that we successfully develop does not achieve broad market acceptance among physicians, patients, health care payors and the medical community, the revenues that it generates from its sales will be limited.

Recent Developments

As of December 31, 2016, we had cash, cash equivalents and marketable securities totaling approximately $17.0 million.

On January 12, 2017, we received $5.0 million pursuant to our exclusive licensing agreement with Kowa Pharmaceuticals America, Inc. described above.

During January 2017, we sold 124,100 shares of our common stock for gross proceeds of $308,202 pursuant to the prospectus supplement relating to the offer and sale of shares pursuant to the Controlled Equity Offering℠ sales agreement with Cantor Fitzgerald & Co. filed with the Securities and Exchange Commission on December 30, 2016.

On January 1, 2017, 1,172,350 shares of common stock were added to the number of shares available for future grant under our 2013 Equity Incentive Plan pursuant to the evergreen provisions of that plan, and in January 2017 our board of directors granted options to acquire 1,016,301 shares of common stock at a weighted average exercise price of $1.72 per share.

Corporate Information

CymaBay Therapeutics, Inc., was incorporated under the laws of the State of Delaware on October 5, 1988, originally under the name Transtech Corporation. Our executive offices are located at 7999 Gateway Blvd., Suite 130 Newark, CA 94560. The telephone number at our executive office is (510) 293-8800. Our corporate website address is www.cymabay.com. We do not incorporate the information contained on, or accessible through, our website into this prospectus, and you should not consider it part of this prospectus. Our website address is included in this prospectus supplement as an inactive textual reference only.

The Offering

Common stock offered by CymaBay	shares
Underwriters' option to purchase additional shares	shares
Common stock to be outstanding after the offering	shares
Use of proceeds	We expect to use the net proceeds from this offering to fund ongoing development of seladelpar and for working capital and general corporate purposes. See "Use of Proceeds" on page S-7 of this prospectus supplement.
NASDAQ Capital Market Symbol	"CBAY"
Risk Factors	Investing in our securities involves a high degree of risk. See the information contained in or incorporated by reference under the heading "Risk Factors" in this prospectus supplement, in the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement and accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering.

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of September 30, 2016. As of that date, we had 23,447,003 shares of common stock outstanding, excluding:

- 2,749,246 shares of common stock underlying options outstanding as of September 30, 2016, at a weighted average exercise price of $5.08 per share;
- 1,667,398 shares of common stock underlying warrants outstanding as of September 30, 2016, at a weighted average exercise price of $5.52 per share;
- 241,080 shares of common stock issuable upon the exercise of outstanding incentive awards at a weighted average exercise price of $5.22 as of September 30, 2016; and
- 466,445 shares of common stock available for future grant under our 2013 Equity Incentive Plan and 2003 Equity Incentive Plan as of September 30, 2016.

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriters in this offering do not exercise their option to purchase up to additional shares of our common stock within 30 days after the date of this prospectus supplement.

RISK FACTORS

Investing in our common stock involves risks. Before making an investment decision, you should carefully consider the risks described below, as well as the information and financial statements contained in the documents incorporated by reference herein, including the risk factors described in our latest Annual Report on Form 10-K and latest Quarterly Report on Form 10-Q. You should consider these risks in light of your particular investment objectives and financial circumstances. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment.

Risks Related to this Offering

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business and cause the price of our common stock to decline.

If you purchase shares of common stock in this offering, you will experience immediate dilution in your investment. You will experience further dilution if we issue additional equity securities in future fundraising transactions.

Purchasers of common stock in this offering will pay a price per share in this offering that exceeds the net tangible book value per share of our common stock. If you purchase shares of our common stock in this offering at the public offering price of $ per share, you will experience immediate dilution of $ per share, representing the difference between the public offering price and our as adjusted net tangible book value per share as of September 30, 2016, after giving effect to this offering. See the section entitled “Dilution” below for a more detailed illustration of the dilution you would incur if you purchase common stock in this offering.

In addition, we have a significant number of stock options and warrants outstanding. To the extent that outstanding stock options or warrants have been or may be exercised or other shares issued, you may experience further dilution.

You may experience further dilution if we issue additional equity securities in future fundraising transactions.

To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering. Further, the exercise of outstanding stock options and warrants may result in further dilution of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements are based on our current expectations, assumptions, estimates and projections about our business and our industry and involve known and unknown risks, uncertainties and other factors that may cause our company's or our industry's results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied in, or contemplated by, the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- our expectations with respect to the clinical development of arhalofenate and our other product candidates, our clinical trials and the regulatory approval process;
- statements regarding the steps, timing and costs of our development programs;
- any projections of earnings, revenue, sufficiency of cash resources or other financial items;
- the plans and objectives of management for future operations;
- the availability of additional financing and access to capital;
- the formation of a trading market for our common stock;
- discussions and approvals of regulatory agencies; and
- the period of time for which we will be able to fund our operations.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the heading "Risk Factors" contained in this prospectus supplement, in any free writing prospectuses we may authorize for use in connection with this offering, and in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q which are incorporated by reference into this prospectus supplement in their entirety. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read this prospectus together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the shares of common stock we are offering will be approximately $ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that the net proceeds to us will be approximately $ million.

We will retain broad discretion over the use of the net proceeds from this offering. We expect to use the net proceeds from this offering to fund ongoing development of seladelpar and for working capital and general corporate purposes. Pending the use of the net proceeds, we expect to invest the net proceeds in investment grade, interest-bearing securities.

DILUTION

Our net tangible book value as of September 30, 2016, was approximately $10.2 million, or $0.44 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2016. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering, and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of our common stock in the aggregate amount of $ at the offering price of $ per share, and after deducting estimated offering commissions and expenses payable by us, our net tangible book value as of September 30, 2016, would have been $ million, or $ per share of common stock. This represents an immediate increase in the net tangible book value per share of $ to our existing stockholders and an immediate dilution in net tangible book value of $ per share to new investors. The following table illustrates this dilution on a per share basis:

Public offering price per share		$
Net tangible book value per share as of September 30, 2016	$0.44	
Increase in net tangible book value per share attributable to investors purchasing our common stock in this offering		
As adjusted net tangible book value per share after this offering		
Dilution per share to investors purchasing our common stock in this offering		$

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of the underwriters' option to purchase up to an additional shares within 30 days of the date of this prospectus supplement or the exercise of other outstanding options and warrants having a per share exercise price less than the public offering price per share in this offering. If the underwriters exercise in full their option to purchase additional shares, our net tangible book value on September 30, 2016, after giving effect to this offering, would have been approximately $ million, or approximately $ per share, representing an immediate dilution of $ per share to new investors purchasing shares of common stock in this offering.

The number of shares of common stock outstanding before and after the offering is based on the number of shares outstanding as of September 30, 2016. As of that date, we had 23,447,003 shares of common stock outstanding, excluding:

- 2,749,246 shares of common stock underlying options outstanding as of September 30, 2016, at a weighted average exercise price of $5.08 per share;
- 1,667,398 shares of common stock underlying warrants outstanding as of September 30, 2016, at a weighted average exercise price of $5.52 per share;
- 241,080 shares of common stock issuable upon the exercise of outstanding incentive awards at a weighted average exercise price of $5.22 as of September 30, 2016;
- 466,445 shares of common stock available for future grant under our 2013 Equity Incentive Plan and 2003 Equity Incentive Plan as of September 30, 2016.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe that we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

CAPITALIZATION

The following table sets forth our capitalization as of September 30, 2016:

- on an actual basis; and
- on an as adjusted basis to reflect the sale by us of shares of our common stock in this offering at the public offering price of $ per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the data set forth in the table below in conjunction with our financial statements, including the related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" from our Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2016, which are incorporated by reference into this prospectus supplement.

	As of September 30, 2016	
	Actual	As adjusted
	(unaudited) (in thousands, except share data)	
Cash, cash equivalents and marketable securities	$ 23,134	$
Warrant liability	1,177	1,177
Facility loan, less current portion	6,809	6,809
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized, no shares issued and outstanding, actual and as adjusted	—	—
Common stock, $0.0001 par value; 100,000,000 shares authorized, 23,447,003 shares issued and outstanding, actual; shares issued and outstanding as adjusted	2	
Additional paid-in capital	426,219	
Accumulated other comprehensive loss	(2)	(2)
Accumulated deficit	(416,007)	(416,007)
Total stockholders' equity	10,212	
Total capitalization	$ 18,198	$

The number of shares of common stock outstanding before and after the offering is based on the number of shares outstanding as of September 30, 2016. As of that date, we had 23,447,003 shares of common stock outstanding, excluding:

- 2,749,246 shares of common stock underlying options outstanding as of September 30, 2016, at a weighted average exercise price of $5.08 per share;
- 1,667,398 shares of common stock underlying warrants outstanding as of September 30, 2016, at a weighted average exercise price of $5.52 per share;
- 241,080 shares of common stock issuable upon the exercise of outstanding incentive awards at a weighted average exercise price of $5.22 as of September 30, 2016;
- 466,445 shares of common stock available for future grant under our 2013 Equity Incentive Plan and 2003 Equity Incentive Plan as of September 30, 2016.

UNDERWRITING

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the shares of common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of common stock set forth opposite their name below. JonesTrading Institutional Services LLC is acting as the representative of the underwriters.

Underwriter	Number of Shares
JonesTrading Institutional Services LLC	
LifeSci Capital LLC	
Total	

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares of common stock sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the overallotment option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares of common stock, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Overallotment Option to Purchase Additional Shares

We have granted to the underwriters an option to purchase up to additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table following the first paragraph of this section.

Underwriting Discounts and Commissions

The following table shows the public offering price, underwriting discount and proceeds, before expenses, to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

We estimate that our total expenses of the offering, excluding the underwriting discount, will be approximately $ and are payable by us, which includes $50,000 for reasonable and documented out-of-pocket expenses incurred by the underwriters in connection with the offering.

		Total	
	Per Share	Without Overallotment	With Overallotment
Public offering price	$	$	$
Underwriting discounts and commissions	$	$	$
Proceeds, before expenses, to us	$	$	$

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the shares to securities dealers at the public offering price less a concession not in excess of $ per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Discretionary Accounts

The underwriters do not intend to confirm sales of the shares of common stock to any accounts over which they have discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase shares of our common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of our common stock while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of shares of our common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that it may purchase in the overallotment option. In a naked short position, the number of shares involved is greater than the number of shares in the overallotment option. The underwriters may close out any short position by exercising the overallotment option and/or purchasing shares of common stock in the open market.
- Syndicate covering transactions involve purchases of shares of our common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares of common stock to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the overallotment option. If the underwriters sell more shares than could be covered by exercise of the overallotment option and, therefore, have a naked short position, the position can be closed out only by buying securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of our common stock in the open market that could adversely affect investors who purchase in the offering.
- Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the shares of common stock originally sold by that syndicate member are purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of shares of our common stock. These transactions may be effected on The NASDAQ Capital Market and, if commenced, may be discontinued at any time.

Passive Market Making

In connection with this offering, the underwriters may engage in passive market making transactions in our common stock on The NASDAQ Capital Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934, as amended, or the Exchange Act, during a period before the commencement of offers or sales of shares and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Lock-up Agreements.

Pursuant to certain "lock-up" agreements, we and our executive officers and directors, have agreed, subject to certain exceptions, not to offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or announce the intention to otherwise dispose of, or enter into any swap, hedge or similar agreement or arrangement that transfers, in whole or in part, the economic consequence of ownership of, directly or indirectly, or make any demand or request or exercise any right with respect to the registration of, or file with the SEC a registration statement under the Securities Act relating to, any common stock or securities convertible into or exchangeable or exercisable for any common stock without the prior written consent of the representative of the underwriters, for a period of 90 days after the date of the pricing of the offering.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. The exceptions to the lock-up for executive officers and directors include: (a) transfers made as a bona fide gift to an immediate family member, to a trust the beneficiaries of which are exclusively the executive officer, director or stockholder or immediate family member, or to a charity or educational institution; (b) transfers made by will or intestate succession; (c) transfers not for value to a shareholder, partner, member or similar equity owner of, or business entity that is an affiliate of, a similar equity interest in, a stockholder that is an entity or to any trustor or beneficiary of a stockholder that is a trust; and (d) the entering into of a written plan meeting the requirements of Rule 10b5-1 under the Securities Exchange Act of 1934. The exceptions to the lock-up for us are: (i) our sale of shares in this offering; (ii) the issuance of common stock or options to acquire common stock pursuant to our employee benefit plans, equity compensation plans or other compensation plans in existence on the date hereof and as described in this prospectus; (iii) the issuance of common stock pursuant to the conversion or exercise of existing securities; and (iv) in connection with the consummation by us of a strategic partnership, joint venture, collaboration or acquisition or license of any business products or technology, provided that the aggregate number of shares does not exceed 5% of the number of shares of common stock outstanding immediately after this offering and the recipient signs a lock-up agreement similar to that signed by our executive officers and directors.

Electronic Offer, Sale and Distribution of Shares

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make Internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships

Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

LifeSci Advisors, LLC, an affiliate of LifeSci Capital LLC, has been retained by us as an investor relations and corporate communications advisor since May 2015. We currently pay a monthly retainer and reimbursement of reasonable out-of-pocket expenses incurred in connection with such engagement. LifeSci Capital LLC was registered as a broker-dealer with the Financial Industry Regulatory Authority in June 2014 and its primary function in connection with the offering contemplated hereby is as underwriter to sell the securities to be registered.

Selling Restrictions

No action has been taken in any jurisdiction except the United States that would permit a public offering of our common stock, or the possession, circulation or distribution of this prospectus or any other material relating to us or our common stock in any jurisdiction where action for that purpose is required. Accordingly, the shares may not be offered or sold, directly or indirectly, and neither this prospectus nor any other offering material or advertisements in connection with the shares may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

Israel. In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 – 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 – 1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the "Addressed Investors"); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 –1968, subject to certain conditions (the "Qualified Investors"). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 – 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 – 1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 – 1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 – 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 – 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

United Kingdom. The underwriters have represented and agreed that:

- it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended), or the

FSMA, except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority, or FSA;

- it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to us; and
- it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

Switzerland. The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area. In relation to each Member State of the European Economic Area (Iceland, Norway and Lichtenstein in addition to the member states of the European Union) that has implemented the Prospectus Directive (each, a Relevant Member State), the underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, or the Relevant Implementation Date, it has not made and will not make an offer of the securities to the public in that Relevant Member State prior to the publication of a prospectus in relation to the securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of the securities to the public in that Relevant Member State at any time:

- to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts; and
- in any other circumstances which do not require the publication by the issuer of a prospectus pursuant to Article 3 of the Prospectus Directive.

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any securities under, the offer contemplated in this prospectus will be deemed to have represented, warranted and agreed to and with us and the underwriter that:

- it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive; and
- in the case of any securities acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, (1) the securities acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the underwriter has been given to the offer or resale; or (2) where securities have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those securities to it is not treated under the Prospectus Directive as having been made to such persons.

For the purposes of the provisions in the two immediately preceding paragraphs, the expression an “offer of the securities to the public” in relation to the securities in any Relevant Member State means the communication

in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State, and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

United Arab Emirates. This document has not been reviewed, approved or licensed by the Central Bank of the United Arab Emirates, or UAE, Emirates Securities and Commodities Authority or any other relevant licensing authority in the UAE including any licensing authority incorporated under the laws and regulations of any of the free zones established and operating in the territory of the UAE, in particular the Dubai International Financial Services Authority, or DFSA, a regulatory authority of the Dubai International Financial Centre, or DIFC. The issue of shares of common stock does not constitute a public offer of securities in the UAE, DIFC and/or any other free zone in accordance with the Commercial Companies law, Federal Law No. 8 of 1984 (as amended), DFSA Offered Securities Rules and the Dubai International Financial Exchange Listing Rules, accordingly or otherwise.

The shares may not be offered to the public in the UAE and/or any of the free zones including, in particular, the DIFC. The shares may be offered and this document may be issued, only to a limited number of investors in the UAE or any of its free zones (including, in particular, the DIFC) who qualify as sophisticated investors under the relevant laws and regulations of the UAE or the free zone concerned. Management of the company and the representatives of the underwriters represent and warrant the shares will not be offered, sold, transferred or delivered to the public in the UAE or any of its free zones.

LEGAL MATTERS

Cooley LLP, Palo Alto, California, will pass upon the validity of the shares of common stock offered hereby. The underwriters are being represented by Goodwin Procter LLP, New York, New York, in connection with the offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2015, as set forth in their report, which is incorporated by reference in this prospectus supplement and accompanying prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus supplement is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information in this prospectus supplement and the accompanying prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement and the accompanying prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement and the accompanying prospectus. We incorporate by reference into this prospectus supplement, the accompanying prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-36500), excluding any portions of any Form 8-K that are not deemed "filed" pursuant to the General Instructions of Form 8-K:

- our Annual Report on Form 10-K for the year ended December 31, 2015, which was filed on March 29, 2016;
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2016, June 30, 2016, and September 30, 2016, which were filed on May 11, 2016, August 9, 2016, and November 9, 2016, respectively;
- our Current Reports on Form 8-K which were filed on January 20, 2016, January 29, 2016, March 22, 2016, March 28, 2016, June 6, 2016, December 8, 2016, January 5, 2017, and January 24, 2017;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2015, referred to above from our definitive proxy statement filed pursuant to Section 14 of the Exchange Act in connection with our 2016 Annual Meeting of Stockholders filed with the SEC on April 21, 2016; and
- the description of our common stock in our registration statement on Form 8-A filed with the SEC on June 16, 2014.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act. Information in such future filings updates and supplements the information provided in this prospectus supplement and the accompanying prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

CymaBay Therapeutics, Inc.
7999 Gateway Blvd., Suite 130
Newark, CA 94560
(510) 293-8800
Attn: Secretary

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PROSPECTUS

$100,000,000
Common Stock
Preferred Stock
Debt Securities
Warrants

From time to time, we may offer and sell up to an aggregate amount of $100,000,000 of any combination of the securities described in this prospectus, either individually or in combination. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants.

We will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered.

Our common stock is listed on the NASDAQ Capital Market under the trading symbol "CBAY." On November 25, 2014, the last reported sale price of our common stock was $7.21 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the NASDAQ Capital Market or other securities exchange of the securities covered by the applicable prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page 6 of this prospectus and any similar section contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

This prospectus may not be used to consummate a sale of securities unless accompanied by a prospectus supplement.

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is November 25, 2014.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration process. Under this shelf registration statement, we may, from time to time, offer and sell, either individually or in combination, in one or more offerings, up to a total dollar amount of $100,000,000 of any combination of the securities described in this prospectus.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to read carefully this prospectus, any applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading "Incorporation of Certain Information by Reference," before buying any of the securities being offered.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

You should rely only on the information contained in, or incorporated by reference into, this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. Neither we nor the selling stockholders have authorized anyone to provide you with different or additional information. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus, the accompanying

prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

The information appearing in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains and incorporates by reference market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe that these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus and the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section entitled “Where You Can Find Additional Information.”

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

CymaBay Therapeutics, Inc.

Overview

CymaBay Therapeutics, Inc. is focused on developing therapies to treat metabolic diseases with high unmet medical need, including serious rare and orphan disorders. Arhalofenate, our lead product candidate, is being developed for the treatment of gout. Arhalofenate has successfully completed three Phase 2 clinical trials in patients with gout and consistently demonstrated the ability to reduce gout flares and reduce serum uric acid (sUA). Gout flares are recurring and painful episodes of joint inflammation that are triggered by the presence of monosodium urate crystals that form as a result of elevated sUA levels. We believe the potential for arhalofenate to prevent or reduce flares while also lowering sUA could differentiate it from currently available treatments for gout. Arhalofenate has established a favorable safety profile in clinical trials involving nearly 1,000 patients exposed to date. We are currently investigating arhalofenate in a 12-week Phase 2b clinical trial in patients with gout and expect to report data from this trial in the second quarter of 2015. Our second product candidate, MBX-8025, demonstrated favorable effects on cholesterol, triglycerides and markers of liver health in a Phase 2 clinical trial in patients with mixed dyslipidemia. We are considering pursuing MBX-8025 in a number of orphan diseases in which these attributes could be beneficial, such as homozygous familial hypercholestorolemia (HoFH), severe hypertriglyceridemia (SHTG) and primary biliary cirrhosis (PBC). We also believe that MBX-8025 could have utility in the treatment of the more prevalent, but high unmeet need, indication of nonalcoholic steatohepatitis (NASH). We plan to initiate one or more pilot or proof-of-concept studies for MBX-8025, beginning with HoFH, in the first half of 2015.

Risks Associated with our Business

Our business is subject to numerous risks. You should read these risks before you invest in our common stock. In particular, our risks include, but are not limited to, the following:

- We will need additional capital in the future to sufficiently fund our operations and research;
- We have incurred significant losses since our inception, we anticipate that we will continue to incur significant losses for the foreseeable future, and we may never achieve or maintain profitability;
- We depend on the success of our lead product candidate, arhalofenate, which is still under clinical development, and MBX-8025, which we currently plan to develop, and may not obtain regulatory approval or successfully commercialize either of these product candidates;
- Our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance;
- We rely on third-party manufacturers to produce our preclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidates;

- We rely on limited sources of supply for the drug substance for our lead product candidate, arhalofenate, and any disruption in the chain of supply may cause delay in developing and commercializing arhalofenate;
- If we are unable to obtain or protect intellectual property rights related to our products and product candidates, we may not be able to compete effectively in our market; and
- Our stock price may be volatile, and our stockholders' investment in our stock could decline in value.

Corporate Information

CymaBay Therapeutics, Inc., was incorporated under the laws of the State of Delaware on October 5, 1988, originally under the name Transtech Corporation. Our executive offices are located at 7999 Gateway Blvd., Suite 130 Newark, CA 94560. The telephone number at our executive office is (510) 293-8800. Our corporate website address is www.cymabay.com. We do not incorporate the information contained on, or accessible through, our website into this prospectus, and you should not consider it part of this prospectus.

As used in this prospectus, "CymaBay," "we," "us," and "our" refer to CymaBay Therapeutics, Inc. and its subsidiaries taken as a whole. The word trademark "CymaBay" is registered on the Principal Register of the United States Patent and Trademark Office. This prospectus also contains trademarks and trade names of other companies, and those trademarks and trade names are the property of their respective owners. We do not intend our use or display of other companies' trademarks or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies or products.

We are an "Emerging Growth Company"

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an "emerging growth company," we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure about our executive compensation arrangements;
- omitted compensation discussion and analysis;
- no requirement that we solicit non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We intend to take advantage of the reduced disclosure obligations. Section 107 of the JOBS Act also provides that an emerging growth company can take advantage of the extended transition period provided in the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. In other words, an emerging growth company can elect to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption to take advantage of the extended transition period for complying with new or revised accounting standards.

We could remain an emerging growth company until the earliest of (i) the last day of the first fiscal year in which our annual gross revenues exceed $1 billion, (ii) the date that we become a "large accelerated filer" as

defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, which would occur if the market value of our common stock that are held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter, (iii) the date on which we have issued more than $1 billion in non-convertible debt during the preceding three-year period and (iv) the last day of the fiscal year following the fifth anniversary of the date of the first sale of our common equity securities pursuant to an effective registration statement under the Securities Act. At this time we expect to remain an "emerging growth company" for the foreseeable future.

CymaBay also qualifies as a "smaller reporting company" and thus has the advantage of not being required to provide the same level of disclosure as larger public companies.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination, up to a total dollar amount of $100,000,000, from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. We may also offer common stock, preferred stock and/or debt securities upon the exercise of warrants. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity date, if applicable;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exercise, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- material or special U.S. federal income tax considerations, if any.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We and the selling stockholders, and our or their agents or underwriters, reserve the right to accept or reject all or part of any

proposed purchase of securities. If we do offer securities to or through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. In this prospectus, we have summarized certain general features of the common stock under "Description of Capital Stock — Common stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. In this prospectus, we have summarized certain general features of the preferred stock under "Description of Capital Stock — Preferred stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

Any debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee.

In this prospectus, we have summarized certain general features of the debt securities under "Description of Debt Securities." We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or in combination with common stock, preferred stock and/or debt securities. In this prospectus, we have summarized certain general features of the warrants under "Description of Warrants." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as any warrant agreements and warrant certificates that contain the terms of the warrants. We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants also may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Use of Proceeds

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital, capital expenditures and other general corporate purposes. See "Use of Proceeds" in this prospectus.

NASDAQ Capital Market Listing

Our common stock is listed on the NASDAQ Capital Market under the symbol "CBAY." The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the NASDAQ Capital Market or other securities exchange of the securities covered by the applicable prospectus supplement.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and discussed under the section entitled "Risk Factors" contained in our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled "Special Note Regarding Forward-Looking Statements."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC that are incorporated by reference contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- our expectations with respect to the clinical development of arhalofenate and our other product candidates, our clinical trials and the regulatory approval process;
- statements regarding the steps, timing and costs of our development programs;
- any projections of earnings, revenue, sufficiency of cash resources or other financial items;
- the plans and objectives of management for future operations;
- the availability of additional financing and access to capital;
- the formation of a trading market for our common stock;
- discussions and approvals of regulatory agencies; and
- the period of time for which we will be able to fund our operations.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the heading "Risk Factors" contained in the applicable prospectus supplement, in any free writing prospectuses we may authorize for use in connection with a specific offering, and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety. Also, these forward-looking statements represent our estimates and assumptions

only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read this prospectus, any applicable prospectus supplement, together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital, capital expenditures and other general corporate purposes, which may include costs of funding future acquisitions or for any other purpose we describe in the applicable prospectus supplement.

BUSINESS

CymaBay Overview

CymaBay Therapeutics, Inc. is focused on developing therapies to treat metabolic diseases with high unmet medical need, including serious rare and orphan disorders. Arhalofenate, our lead product candidate, is being developed for the treatment of gout. Arhalofenate has successfully completed three Phase 2 clinical trials in patients with gout and consistently demonstrated the ability to reduce gout flares and reduce serum uric acid (sUA). Gout flares are recurring and painful episodes of joint inflammation that are triggered by the presence of monosodium urate crystals that form as a result of elevated sUA levels. We believe the potential for arhalofenate to prevent or reduce flares while also lowering sUA could differentiate it from currently available treatments for gout. Arhalofenate has established a favorable safety profile in clinical trials involving nearly 1,000 patients exposed to date. We are currently investigating arhalofenate in a 12-week Phase 2b clinical trial in patients with gout and expect to report data from this trial in the second quarter of 2015. Our second product candidate, MBX-8025, demonstrated favorable effects on cholesterol, triglycerides and markers of liver health in a Phase 2 clinical trial in patients with mixed dyslipidemia. We are considering pursuing MBX-8025 in a number of orphan diseases in which these attributes could be beneficial, such as homozygous familial hypercholestorolemia (HoFH), severe hypertriglyceridemia (SHTG) and primary biliary cirrhosis (PBC). We also believe that MBX-8025 could have utility in the treatment of the more prevalent, but high unmeet need, indication of nonalcoholic steatohepatitis (NASH). We plan to initiate one or more pilot or proof-of-concept studies for MBX-8025 in the first half of 2015.

We believe arhalofenate has the potential to address unmet needs in the treatment of gout. Of the eight million patients with gout in the U.S., we estimate that over three million are on urate lowering therapy (ULT). Approximately one million of these patients on ULT continue to experience three or more flares per year, with significant impact to patient quality of life and the health care system. This patient population is poorly served by available therapies. The two primary goals of gout treatment are the prevention of flares and lowering of sUA. The fundamental limitation in achieving these goals is that all currently available ULTs cause an increase in flares upon initiation of treatment, leading many patients to discontinue or avoid therapy. Given this increase in flares, standard of care includes prophylaxis with colchicine and use of anti-inflammatory medications, which are often poorly tolerated or inadvisable for use in gout patients due to their side effects. Despite prophylaxis with colchicine, many patients continue to experience flares. We believe that by decreasing flares while lowering

sUA, arhalofenate has the potential to treat patients with gout without the need for colchicine or other anti-inflammatory medications and would thus be differentiated from all currently available gout therapies.

CymaBay Strategy

Our goal is to become a leading biopharmaceutical company focused on developing and commercializing proprietary new medicines for metabolic and rare diseases with high unmet need. Key elements of our strategy are to:

- develop arhalofenate as a dual-acting treatment to prevent or reduce flares and lower sUA in patients with gout;
- develop MBX-8025 for high unmet need or orphan indications linked to defects in lipid storage, handling and utilization and certain diseases effecting liver function;
- pursue partnerships to advance and commercialize arhalofenate and potentially other clinical candidates; and
- strengthen our patent portfolio and other means of protecting exclusivity.

CymaBay Pipeline Overview

Our pipeline includes three unpartnered clinical stage product candidates and a number of preclinical programs.

Arhalofenate—Gout

Gouty arthritis, or simply gout, is the most common form of inflammatory arthritis in men and affects more than eight million people in the United States (U.S.). The hallmark symptom of gout is a flare, characterized by debilitating pain, along with tenderness and inflammation of affected joints. Gout has a significant impact on patients' quality of life and health care utilization. Patients experiencing gout flares miss an average of 4.6 more days of work per year than those without gout. Gout flares also result in increased health care utilization with approximately 35% of moderate and 50% of severe gout patients who experience a flare having at least one acute care visit per year.

Gout flares are recurring and painful episodes of joint inflammation that are triggered by the presence of monosodium urate (MSU) crystals. MSU crystals are formed in tissues when the concentration of serum uric acid (sUA) exceeds its solubility limit of approximately 6.8 milligrams per deciliter (mg/dL). Elevated levels of sUA, or hyperuricemia, most commonly results from the under excretion of uric acid in the kidney. This is caused by its reabsorption from urine and transport back to the blood by specialized urate transporters/exchangers in the proximal renal tubule. Long term accumulation of MSU crystals in the body leads to the progression of gout with an increase in the frequency of flares, the involvement of multiple joints, the formation of visible masses of MSU crystals (tophi) and the debilitation that results from deformation of joints.

Many scientific surveys and large clinical studies in gout indicate that gout patients have a high incidence of cardiovascular and metabolic comorbidities, such as hypertension (50% or more), coronary artery disease (>35%), chronic kidney disease (~40%), and diabetes (~20%). Managing patients with these comorbidities is challenging because many of them are contraindicated in the medication currently used to treat gout. Examples include corticosteroids which can cause hypertension and worsening of dysglycemia and non-steroidal anti-inflammatory drugs (NSAIDs) which have renal toxicity.

Market Opportunity

Unmet Needs in the Treatment of Gout

Of the eight million patients with gout in the U.S., we estimate that over three million are on urate lowering therapy (ULT) and of these patients on ULTs, about one million will continue to experience three or more flares per year, with significant impact to patient quality of life and the health care system. According to a 2012 study, patients having three or more flares per year typically incur $10,000 more in annual health care costs than patients without gout. In order to halt the progression of the disease and provide long term reduction in flares, MSU crystals must be eliminated from the body. Therefore, the two major goals of gout treatment are to prevent flares and lower sUA to below 6 mg/dL in order to dissolve MSU crystals present in tissue. The most important limitation in achieving these goals is that all existing ULTs paradoxically cause an increase in flares upon initiation of treatment, leading many patients to discontinue or avoid therapy. Non-adherence to therapy is a significant problem. In one long term study, only about 40% of allopurinol patients reached the goal of sUA < 6 mg/dL (Febuxostat Briefing Package FDA Advisory Committee Meeting November 24, 2008). Failure to get to goal results in progression of the disease and continued flaring.

Limitations of Current Therapies

Allopurinol and febuxostat (marketed by Takeda Pharmaceutical Company Limited as Uloric®), the most common drugs prescribed to lower sUA, increase flares for up to 6 – 12 months following initiation of treatment. The ULT-initiated flare phenomenon is common to marketed ULTs and leads to increased health care utilization and high patient discontinuation with progression of disease.

To address the increase in flare rate associated with initiation of ULT therapy, anti-inflammatory drugs such as colchicine and NSAIDs are co-prescribed with ULTs. However, use of these agents carries a risk for causing adverse effects. Some known adverse effects of colchicine include diarrhea, nausea, vomiting, destruction of skeletal muscle, neuromuscular toxicity, and decreased blood cell production. Chronic use of NSAIDs, which only provide symptom relief, is associated with increased risk of renal toxicity, gastrointestinal (GI) bleeding and cardiovascular events. Similarly, steroids are linked to hypertension and a worsening of blood glucose, which is problematic for diabetics and patients with hypertension and/or heart disease, respectively. Given the prevalence of cardiovascular and metabolic comorbidities in gout patients, the use of these agents can be problematic in a significant number of gout patients.

Anti-Flare Competition

The largest selling branded gout drug in the U.S. is Colcrys® (branded colchicine), marketed by Takeda for the prevention and treatment of gout flares. Despite the availability of low cost generic NSAIDs and steroids, Colcrys had total U.S. sales of approximately $629 million in 2013 per IMS Health data highlighting the importance of preventing and treating gout flares effectively. While colchicine has been shown to reduce the percentage of patients experiencing flares by 57%, it carries limitations in terms of safety and tolerability.

The biologic drugs Ilaris (developed by Novartis) and Arcalyst (developed by Regeneron) which neutralize the proinflammatory cytokine IL-1ß, the trigger for flares, have been shown in clinical trials to suppress gout flares. However, there are safety risks associated with these drugs, and neither drug has gained approval in the U.S. for gout.

Serum Uric Acid Lowering Competition

Xanthine oxidase (XO) inhibitors, allopurinol and febuxostat, dominate the ULT market with generic allopurinol at doses up to 300 mg accounting for about 90% of ULT prescriptions in the U.S. Allopurinol may potentially lead to undertreatment because of the occurrence of skin rash and a rare but serious hypersensitivity reaction which can be fatal. In addition, it must be used with caution in renally impaired patients, a common

comorbidity in gout, and is recommended to undergo dose escalation. Febuxostat, approved by the Food and Drug Administration (FDA) in 2009, was the first new treatment approved for gout in more than 40 years.

Lesinurad is a drug in Phase 3 development by AstraZeneca PLC. Like arhalofenate, it lowers sUA by promoting the excretion of uric acid by the kidney. However, lesinurad, like all other ULTs, has been shown to increase flares upon initiation of treatment. Lesinurad is being studied as an add-on treatment to allopurinol patients not reaching target sUA levels, as an add-on to febuxostat in tophaceous gout patients and as monotherapy (given as a single drug) for patients who are intolerant to XO inhibitors.

While medically important, we believe the case for sUA lowering alone is not sufficient to ensure success in the market because hyperuricemia is asymptomatic and patients usually seek treatment for their flares.

Arhalofenate Addresses the Unmet Needs in Gout

We believe that a significant opportunity exists for arhalofenate as a result of its combined anti-flare and sUA lowering profile for the treatment of gout. Arhalofenate has the potential to address key unmet needs by preventing flares and achieving sUA target goals as monotherapy. In patients who need additional sUA lowering, arhalofenate may be combined with other ULTs to significantly reduce sUA without the induction of flares seen with other ULTs.

We have undertaken an analysis of the gout market expected at the time of arhalofenate's launch. Arhalofenate has dual pharmacology, whereas other gout drugs on the market or in development, are limited to only either anti-flare or sUA lowering. Given arhalofenate has demonstrated the ability in our Phase 2 studies to reduce and prevent flares while also lowering sUA, we believe it has the potential to be the preferred alternative for the approximately 1 million patients who flare three or more times per year despite being on ULT. We believe the poor compliance of patients treated with existing ULTs also leads to more than one million discontinuations and restarts of therapy every year. The cycling of patients on and off ULTs would offer opportunities for physicians to switch patients on other therapies to arhalofenate.

As a monotherapy, we believe arhalofenate has the potential to be a single, safe, easy-to-use replacement for the combination of allopurinol and colchicine, which is the current standard of care.

For those patients needing additional sUA reduction, our clinical trial data have demonstrated that arhalofenate has the potential to be combined with febuxostat to provide large (~60%) reductions in sUA, but without the large increases in the incidence of flares seen with all other ULTs.

Arhalofenate Overview

Scientific Rationale

Arhalofenate is a prodrug which upon absorption is converted to its active form, arhalofenate acid. Arhalofenate acid's dual actions are to block the MSU crystal-stimulated production of IL-1ß by macrophages (white blood cells that play an important role in the body's defense against pathogens and foreign matter) in joints and to inhibit uric acid reabsorption by urate transporters in the kidney.

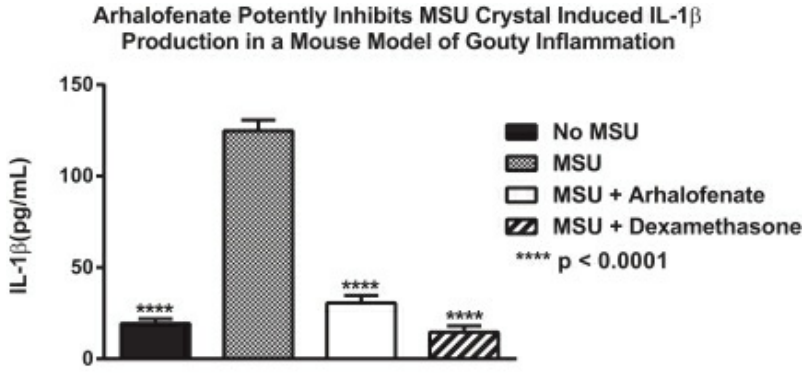
Anti-Inflammatory Activity

We believe, arhalofenate (through arhalofenate acid) is unique among available anti-inflammatory drugs because it prevents the initiation of the inflammatory cascade and acts upstream from other therapies used for the prophylaxis and treatment of gout flares. The anti-inflammatory action comes from a unique trans-repression (a type of inhibition) of peroxisome proliferator-activated receptor-gamma (PPARg) which blocks the production of IL-1ß and other inflammatory proteins by macrophages that produce a flare. Neutralization of IL-1ß has been

shown in clinical trials to reduce flares by about 70%. Because arhalofenate acid acts upstream of colchicine, it may be able to replace colchicine.

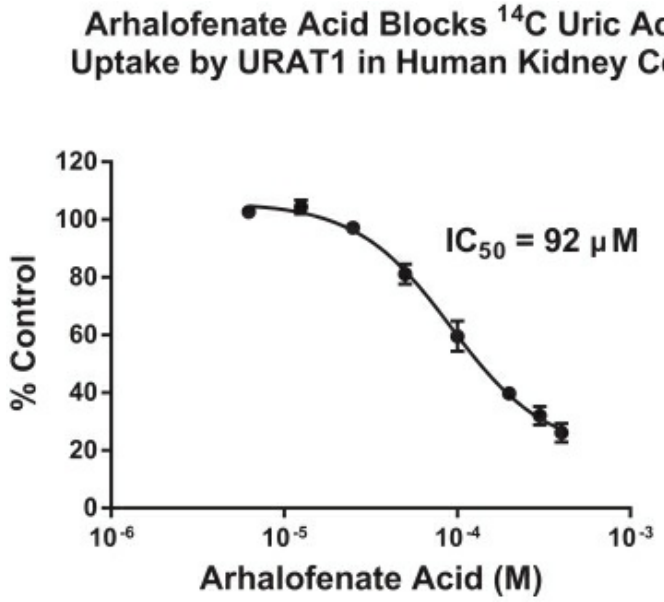
The anti-inflammatory mechanism of arhalofenate acid has been demonstrated in preclinical models. In experiments with isolated macrophages, arhalofenate acid is able to suppress MSU crystal-stimulated release of IL-1ß protein by blocking expression of the precursor pro-IL-1ß gene. Importantly, this activity is seen at concentrations that are achieved in humans.

In vivo confirmation of this effect was seen in a mouse model of gouty inflammation. Injecting MSU crystals into mice produces many of the molecular and cellular steps involved in a gout flare. As shown below, administration of arhalofenate at doses that produce clinically relevant exposures was able to suppress the release of IL-1ß in response to MSU crystals to a degree similar to that of dexamethasone, a potent anti-inflammatory steroid drug. Importantly, it also suppresses other important inflammatory mediators, such as CXCL1, CXCL2 and MCP-1 (chemokine (C-X-C motif) ligand 1 and ligand 2 and monocyte chemotactic protein 1), that colchicine does not.



Uric Acid Lowering Activity

Uric acid is an anionic, or negatively charged, molecule that is removed from the body by filtration through the kidney into urine. For about 80-90% of patients, hyperuricemia is a result of under excretion of uric acid due to its reabsorption by organic anion transporters (OAT) in the proximal renal tubule. Arhalofenate acid blocks ^{14}C-uric acid uptake in an embryonic kidney cell line that expresses human urate transporter 1 (URAT1), one of the predominant renal transporters of urate. The inhibition is pharmacologically relevant because it occurs at concentrations that are less than those seen in human urine in clinical trials. Arhalofenate acid was shown to inhibit uric acid uptake by URAT1, OAT4 and OAT10, three of the transporters that play a critical role in uric acid reabsorption. This mechanism is consistent with the clinical pharmacology in which arhalofenate was shown to dose-dependently increase urate clearance into urine in gout patients.



The available preclinical evidence provides an explanation for the dual mode-of-action observed for arhalofenate in treating gout patients. CymaBay has completed three clinical studies in gout patients which have shown that arhalofenate has the potential for both decreasing the incidence, severity and duration of gout flares, including those that often occur upon initiation of ULT, and reducing sUA.

CymaBay has completed a nonclinical program for arhalofenate, including genotoxicity, chronic repeat dose toxicology in rats and monkeys, safety pharmacology, reproductive toxicology and two-year rodent carcinogenicity studies. The results of these studies have all been submitted to and received by the FDA.

CymaBay has developed a manufacturing process for arhalofenate and ~200 kg of drug substance is available to initiate the Phase 3 program. Tablets for the Phase 2b study have already been manufactured. Both the drug substance and tablet manufacturing processes will be scaled up to support the registration and commercial chemistry, manufacturing and controls program.

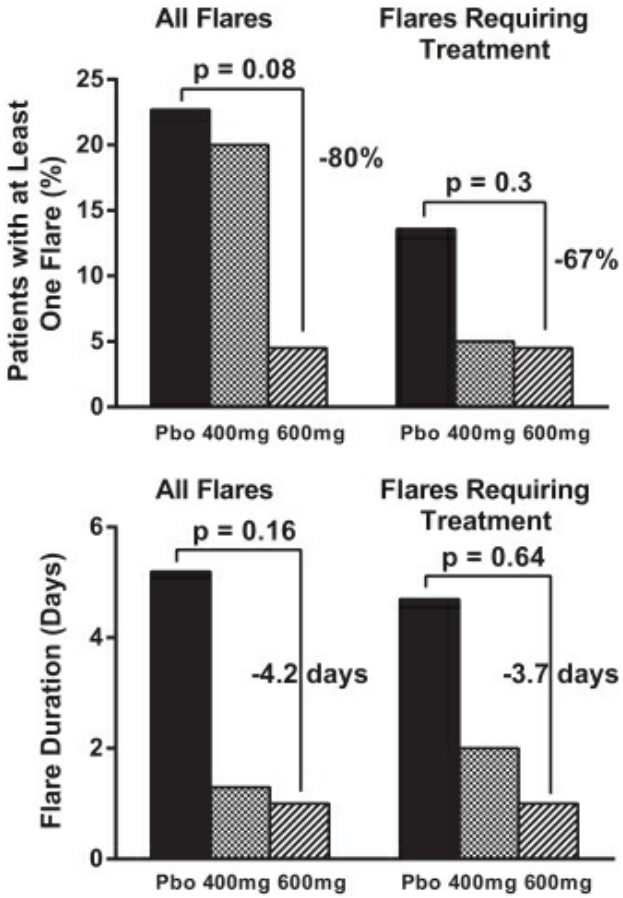
Clinical Studies with Arhalofenate

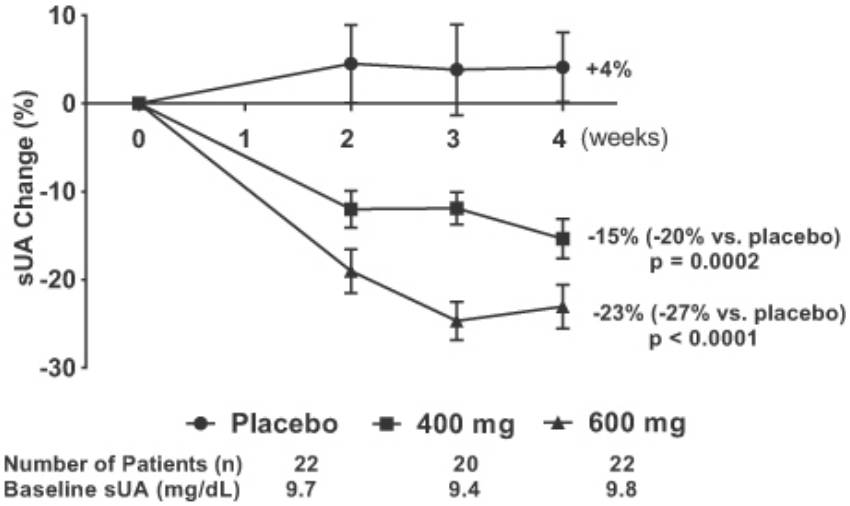
The Gout Development Program

Arhalofenate has been studied in three Phase 2 gout clinical trials including a monotherapy study, febuxostat combination study and an allopurinol combination study.

Monotherapy Study

The monotherapy study was a randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of arhalofenate for the treatment of hyperuricemia in patients with gout. Arhalofenate was given daily at doses of 400 mg and 600 mg for four weeks. A total of 64 patients completed the treatment phase: 22 received placebo, 20 received arhalofenate 400 mg, and 22 received arhalofenate 600 mg. All randomized patients also received colchicine 0.6 mg daily as flare prophylaxis, a preventive treatment for flares. Compared to placebo, patients treated with arhalofenate demonstrated dose-dependent reductions in gout flare and sUA, as shown below. The proportion of patients reporting at least one flare during the treatment phase was 23% (5 of 22), 20% (4 of 20), and 5% (1 of 22) in the placebo, 400 mg, and 600 mg groups, respectively. In addition to flare frequency, both severity and duration of flare were lower in arhalofenate-treated patients. After 4 weeks of treatment, the mean sUA percent (and absolute) changes from Day 1 were: +4% (+0.2 mg/dL) in the placebo group, -15% (-1.4 mg/dL) in the 400 mg arhalofenate group and -23% (-2.3 mg/dL) in the 600 mg arhalofenate group. When compared to placebo, the sUA reductions in both arhalofenate treatment groups were statistically significant (p£0.0002).



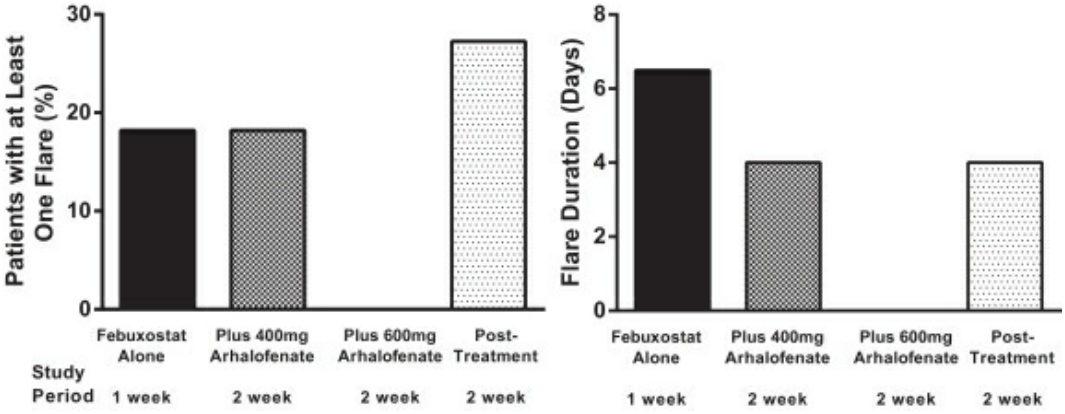


Overall, adverse events (AEs) were similar among the placebo and arhalofenate-treated groups. There were no severe or serious AEs, discontinuations due to AEs, or deaths during the study. Overall, the types and frequencies of AEs were similar among patients receiving placebo or arhalofenate 400 mg or 600 mg and there were no clinically meaningful differences observed in safety laboratory test results.

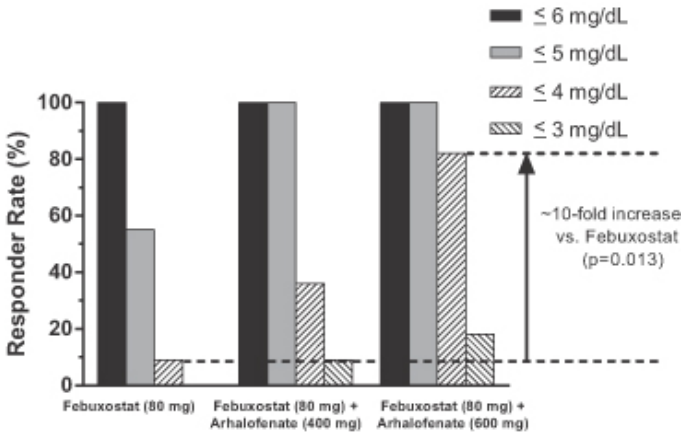
Febuxostat Combination Study

In the febuxostat combination study, arhalofenate up to 600 mg daily was added to febuxostat 80 mg in an open-label, in-patient study to determine the efficacy, safety, and tolerability of arhalofenate in combination with 80 mg febuxostat once daily. A total of 11 patients were dosed with 80 mg febuxostat during Week 1, 80 mg febuxostat plus 400 mg arhalofenate during Weeks 2-3 and 80 mg febuxostat plus 600 mg arhalofenate during Weeks 4-5. All patients also received 0.6 mg colchicine daily as prophylaxis for gout flare.

The proportion of these patients reporting at least one flare was 18% (2 of 11 patients) during Week 1 (febuxostat 80 mg) and 18% (2 of 11 patients) during Weeks 2-3 (febuxostat 80 mg plus arhalofenate 400 mg), respectively. No patient reported the initiation of a flare during Weeks 4-5 (febuxostat 80 mg plus arhalofenate 600 mg). The proportion of patients reporting at least one flare in the two-week follow-up period was 27% (3 of 11 patients).



Mean sUA reductions were -48% at Day 8 (febuxostat 80 mg), -54% at Day 22 (febuxostat 80 mg plus arhalofenate 400 mg), and -60% at Day 36 (febuxostat 80 mg plus arhalofenate 600 mg). Historically, one week of dosing with febuxostat 80 mg has been shown to give the full effect of sUA reduction, and the mean reductions in this study at Day 8 are consistent with other reported study results. The proportion of patients who achieved various sUA target levels during treatment is shown below. Patients with advanced gout have large stores of MSU crystals in the body, and driving sUA levels to lower values (e.g., < 4 mg/dL) has been shown with other ULTs to accelerate clinical benefits such as the reduction of tophi (masses of MSU crystals).



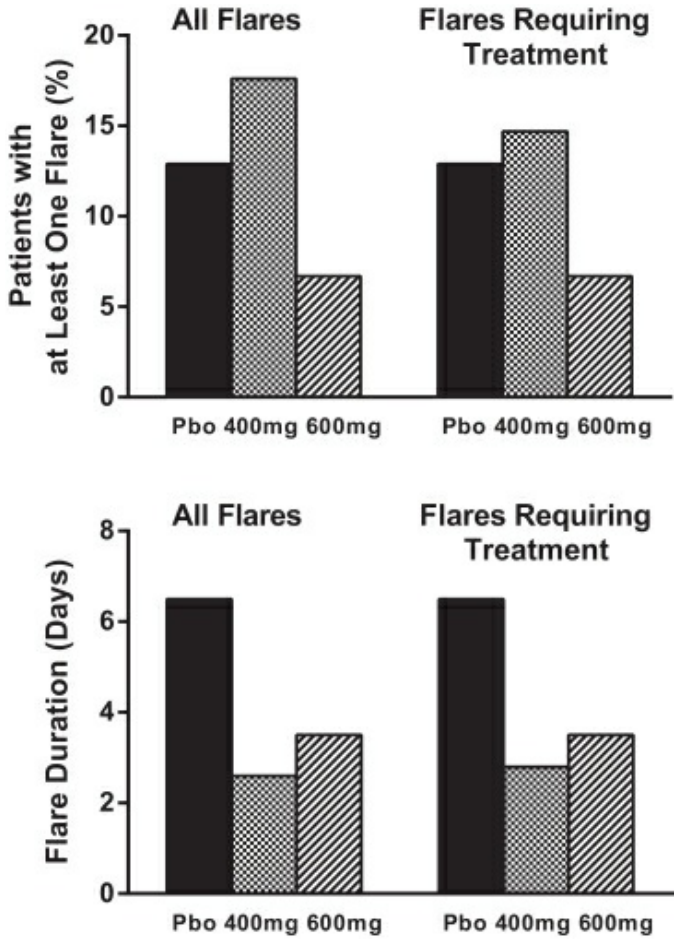
No patients experienced severe or serious AEs or deaths, and there were no discontinuations because of AEs. No clinically meaningful differences were observed among the study treatments in safety laboratory test results.

Allopurinol Combination Study

This study was a randomized, double-blind, placebo-controlled clinical trial designed to evaluate the efficacy, safety and tolerability of arhalofenate 400 mg and 600 mg when given in combination with allopurinol 300 mg and also to evaluate the effect of arhalofenate on the pharmacokinetics (PK, drug levels in the blood) of allopurinol and oxypurinol, (the product of metabolism or active metabolite of allopurinol) that forms in the body after ingestion of allopurinol. Arhalofenate (or placebo) was given once daily at doses of 400 mg and 600 mg, in addition to allopurinol 300 mg, for four weeks to patients who had failed to reach the sUA target of <6 mg/dL with allopurinol 300 mg. All randomized patients also received colchicine 0.6 mg daily as flare prophylaxis. A reduction in gout flares was observed in the arhalofenate 600 mg plus allopurinol group compared to the allopurinol only group. The proportion of patients in a pre-specified per protocol population reporting at least one flare during the 4-week treatment phase was 13% (4 of 31) in the allopurinol 300 mg only group, 18% (6 of 34) in the allopurinol 300 mg plus arhalofenate 400 mg group, and 7% (2 of 30) in the allopurinol 300 mg plus arhalofenate 600 mg group. The mean duration of flares was longer in the allopurinol plus placebo group (6.5 days) than in either the allopurinol plus 400 mg arhalofenate group (2.6 days) or the allopurinol plus 600 mg arhalofenate group (3.5 days).

There was no statistically significant difference in sUA reduction in the arhalofenate plus allopurinol groups compared to the allopurinol only group. In the per protocol population, the proportion of patients who reached a sUA target of <6 mg/dL at the end of the treatment phase was 35.5%, 52.9%, and 43.3% in the allopurinol plus placebo group, the allopurinol plus 400 mg arhalofenate group, and the allopurinol plus 600 mg arhalofenate group, respectively. The modest additional sUA reduction observed in the arhalofenate plus allopurinol groups in this study is attributable to an interaction in which arhalofenate reduces the concentration of oxypurinol, the active metabolite of allopurinol. Specifically, arhalofenate promotes the excretion of uric acid as well as

oxypurinol given both are typically reabsorbed into the blood stream through the same renal transporters arhalofenate is responsible for blocking.



No severe or serious AEs were reported. Two patients discontinued from the study due to moderate AEs. Overall, the types and frequencies of AEs were similar among the treatment groups and there were no clinically meaningful differences observed among the study treatments in safety laboratory test results.

Prior Clinical Experience with Arhalofenate

Prior to the Phase 2 trials in gout described above, eight Phase 1 studies and four Phase 2 studies in patients with type 2 diabetes mellitus (T2DM) were conducted with arhalofenate. In these studies a total of 873 subjects were studied. Daily treatment with arhalofenate up to 600 mg for up to 24 weeks in T2DM patients was found to be safe and well tolerated. Prior to conducting the third and fourth Phase 2 clinical studies in patients with T2DM, we entered into an exclusive licensing agreement for arhalofenate with Ortho-McNeil in June 2006.

In these T2DM studies, daily treatment with arhalofenate with doses up to 600 mg for up to 24 weeks duration showed improvements in glucose parameters (hemoglobin A1c [HbA1c] and fasting plasma glucose), as well as a lowering of serum triglycerides in patients with elevated levels at baseline. However, given that the observed reductions in HbA1c and fasting plasma glucose were inferior for patients receiving arhalofenate versus for those receiving the comparator drug, Actos™, arhalofenate's development for diabetes was abandoned.

Ortho-McNeil terminated the license in March 2010 and has no further rights to arhalofenate. Arhalofenate was found to be well tolerated with no meaningful treatment group differences in AEs including those of special interest (edema, weight gain, and upper GI AEs), discontinuation due to AEs, serious AEs, and death. There were no reports of urinary tract stones in any of these studies. No clinically meaningful differences were observed in safety laboratory test results including LFTs and serum creatinine values between placebo and arhalofenate-treated groups. Patients with LFT increase did not demonstrate any increase in serum bilirubin; therefore, no patient met the criteria of Hy's law of drug induced liver injury.

A pooled analysis of sUA data from these diabetes studies showed statistically significant dose dependent reductions from baseline in mean sUA with arhalofenate: +2% in the placebo group (n=252), -11% in the 200 mg group (n=125), -20% in the 400 mg group (n=174), and -27% in the 600 mg group (n=159); $p<0.0001$ for each active group vs. placebo comparison. A p-value is a statistical measure of the probability that the difference in two values could have occurred by chance. The smaller the p-value the greater the confidence that the results are significant. For example, in the preceding studies, there is less than a 0.01% probability that the difference between two values is due to chance and, conversely there is a 99.99% probability that the observed difference was not due to chance. Similar sUA reduction was observed in patients with mild to moderate renal impairment and without additional worsening of renal function. Comparable sUA reduction was also achieved with arhalofenate in patients on concomitant low-dose aspirin (up to 325 mg daily) and on diuretics (blood pressure lowering agents).

Conclusions of Arhalofenate's Clinical Experience

Arhalofenate has been studied in a total of 15 clinical trials with nearly a thousand subjects. These include Phase 1 studies of safety, tolerability and PK, Phase 2 studies of blood glucose effects in diabetics, and Phase 2 studies of sUA and flare effects in gout patients. Arhalofenate has had a consistent pattern of good safety and tolerability. Despite having differing objectives across these studies, arhalofenate demonstrated comparable dose-dependent reductions in sUA.

In addition to its primary characteristics for reduction of flare incidence and duration and in sUA lowering, arhalofenate also has additional features which are important in the gout population. It has shown an ability to lower triglycerides in subsets of patients with elevated serum triglycerides and to improve blood glucose parameters in diabetics, which are common comorbidities in gout patients. In an exploratory analysis, it retained its ability to lower sUA in patients with impaired renal function, another highly prevalent comorbidity in gout patients. In addition, arhalofenate gave comparable reductions in sUA whether or not patients were on low dose aspirin or thiazide diuretic (first-line therapy for uncomplicated hypertension) therapies, these latter agents being known to exacerbate hyperuricemia and to sometimes trigger flares when their treatment is initiated.

In the treatment of over a hundred patients with hyperuricemia and a diagnosis of gout, arhalofenate was safe and well tolerated and produced a consistent reduction in flare incidence and duration and in lowering sUA whether administered alone or in combination with allopurinol 300 mg or febuxostat 80 mg. The time-course of reductions in sUA was gradual and favorable for those of a drug intended to treat gout in which rapid fluctuations in sUA levels are inadvisable. It was shown as a single agent to dose-dependently increase urate excretion and fractional urate clearance, establishing that its sUA mechanism is uricosuria (i.e., it is a uricosuric).

Clinical Development of Arhalofenate for Treatment of Gout

Current Phase 2b Study

The goal of our current Phase 2b study is to investigate the full potential benefit of arhalofenate monotherapy with regard to flare prevention and sUA lowering in a more robust, longer trial. Importantly, we are investigating the benefits of two doses of arhalofenate monotherapy, including a higher dose than we studied in previous gout studies, without colchicine.

This randomized, double-blind, active comparator- and placebo-controlled study will evaluate the safety, flare prevention and sUA-lowering activity of arhalofenate in approximately 250 patients with a diagnosis of gout hyperuricemia and a history of 3 or more flares in the last 12 months. The study has 5 arms including placebo, arhalofenate (600 and 800 mg), allopurinol (300 mg) and allopurinol (300 mg) plus colchicine (0.6 mg). The primary endpoint of the study is the flare incidence rate for the arhalofenate (800 mg) arm vs. allopurinol (300 mg) following twelve weeks of treatment. A key secondary endpoint is the sUA responder rate (the percentage of patients that achieve sUA levels below 6 mg/dL) for the treatment arms. The study is designed to assess whether arhalofenate can provide sUA lowering comparable to the most commonly prescribed dose of allopurinol (300 mg) and flare reduction similar to colchicine.

We began enrollment in our Phase 2b study in March 2014 and announced completion of enrollment on September 29, 2014. We expect to report data from this study in the second quarter of 2015.

Phase 3 Gout Program

The details (design, size, duration, etc.) of the Phase 3 program will be the subject of discussion at an End-of-Phase 2 meeting with the FDA, and will be designed to support an indication for both arhalofenate monotherapy and combination treatment with febuxostat.

In order to support this indication, and the broad use of arhalofenate to both prevent flares and reduce sUA, the Phase 3 clinical program is currently planned to include two pivotal gout studies: one arhalofenate monotherapy study, and one study of arhalofenate in combination with febuxostat. These will both be randomized, double-blind studies, with appropriate controls and statistical power. The program will also include a single arm, open label safety study to accumulate additional longer term safety data needed for the New Drug Application (at least 100 patients dosed for at least one year at the proposed dose). A small number of Phase 1 studies, including necessary drug-drug interaction studies, or special population studies, will also be conducted prior to registration.

MBX-8025

MBX-8025 is a selective agonist (a substance that elicits a response by binding to a receptor) for the peroxisome proliferator-activated receptor delta (PPARd). PPARd is a nuclear receptor that regulates genes involved in lipid storage, transport and metabolism (particularly fatty acid oxidation) and in insulin signaling and sensitivity. MBX-8025 has the potential to treat a variety of disorders characterized by derangements in lipid metabolism and certain diseases of the liver. Previously, MBX-8025 had been in development as a treatment for mixed dyslipidemia (elevated LDL-C and triglycerides (TGs) and often associated with decreased HDL-C). Results from our Phase 2 clinical trial of MBX-8025 in patients with mixed dyslipidemia established a number of clinically and statistically significant effects of the drug that we believe have the potential to benefit patients affected with other conditions. In this trial, MBX-8025 demonstrated an anti-atherogenic profile in which it lowered LDL-C, decreased the more atherogenic (i.e. tending to promote the formation of fatty plaques in the arteries) small dense LDL-C particles and raised HDL-C. In addition, MBX-8025 decreased TGs and free fatty acids. Whereas other lipid lowering drugs lower either TGs or LDL-C or predominantly act on one of these parameters, MBX-8025 has been shown in this trial to lower both at the same time. Treatment with MBX-8025 also led to significant decreases in gamma-glutamyl transferase (GGT), an enzymatic biomarker that has been associated with the liver inflammation that is often associated with the accumulation of fat in the liver (steatosis). Finally, treatment with MBX-8025 resulted in significant reductions in alkaline phosphatase (AP), an enzymatic biomarker associated with liver cholestasis.

Despite these positive results, we have decided not to further develop MBX-8025 for mixed dyslipidemia because of the requirement by the FDA to conduct a preapproval cardiovascular outcome study for all novel drugs in mixed dyslipidemia. This significantly increases the risk, time and cost of development for this indication.

Another factor in our decision to redirect development relates to an issue specific to compounds that work by interacting with the PPAR class of receptors (PPARa, PPARg and PPARd), including MBX-8025. These compounds are subject to a FDA partial clinical hold which limits clinical studies to durations of less than six months until the two-year rodent carcinogenicity studies are completed and evaluated, and the hold is lifted. The decision by the FDA to lift the partial hold involves an assessment of the human relevance and perceived risk of the rodent carcinogenicity findings in relation to the benefit to the patient for the intended indication. We have completed the two-year rodent carcinogenicity studies with MBX-8025 as well as some additional follow-up studies requested by the FDA. After completion of clinical studies for HoFH or other indications described below, the FDA has indicated that they will determine whether to lift the partial hold based on the risk-benefit profile for the patient.

For these reasons, we have decided to redirect the development of MBX-8025 for serious rare and orphan diseases or more prevalent diseases with high unmet medical need for which the risk/benefit assessment of the carcinogenicity findings would be more favorable to the patient and where an outcome study would not be necessary. We have identified a number of such indications in which there is a clear scientific rationale to suggest that the beneficial effects of MBX-8025 observed in our mixed dyslipidemia trial may be retained in that disease population. We believe MBX-8025 may provide a significant benefit for patients across a wide range of rare diseases associated with disorders of lipid metabolism, such as homozygous familial hypercholesterolemia (HoFH) and severe hypertriglyceridemia (SHTG) syndromes, and disorders of liver function, such as primary biliary cirrhosis (PBC). We also believe that MBX-8025 could have utility in the treatment of the more prevalent, but high unmeet need, indication of nonalcoholic steatohepatitis (NASH).

Nonclinical Overview

In *in vitro* studies with cells and animal tissues, MBX-8025 was shown to up-regulate genes involved in the metabolism and handling of lipids, most notably stimulation of fatty acid transport and oxidation.

In preclinical studies in rodents, dogs and primates, MBX- 8025 demonstrated a variety of beneficial effects on the lipid profile and other metabolic parameters. MBX-8025 treatment increased peripheral oxidation of fatty acids leading to reduced levels of TGs and LDL-C, while raising HDL-C. MBX-8025 also inhibited fat mass accumulation, resulting in attenuation of body weight gain in rodent models of obesity.

Three-month toxicology studies in rodents (alone and in combination with atorvastatin, the generic name of the cholesterol lowering drug Lipitor®) and in monkeys have been completed. In addition, the two-year carcinogenicity studies in mice and rats have been completed. Johnson & Johnson Pharmaceutical Research & Development filed an IND for this compound with the FDA in July 2005 and subsequently transferred the application to CymaBay in March 2007.

Clinical Trials with MBX-8025

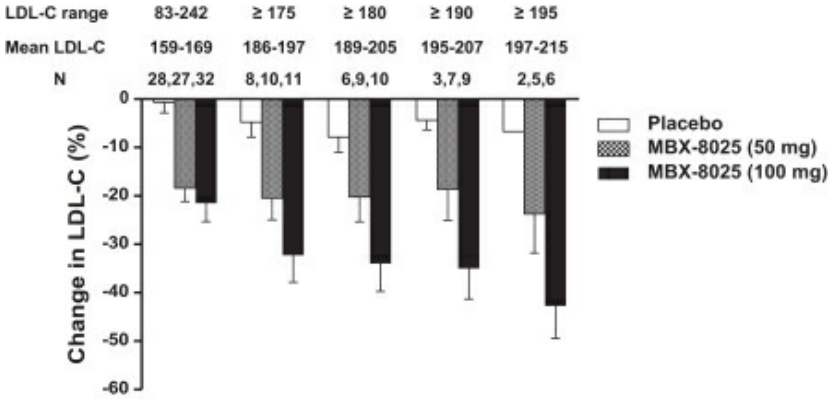
Five Phase 1 and one Phase 2 clinical trials with MBX-8025 have been completed. The largest clinical trial was an eight-week, Phase 2 trial in which MBX-8025 was administered at doses of 50 or 100 mg/day both alone and in combination with 20 mg/day of atorvastatin in moderately obese patients with mixed dyslipidemia. This trial also had a placebo arm and a 20 mg/day atorvastatin only arm.

Treatment with MBX-8025 produced multiple beneficial effects on lipid parameters. First, there were significant overall reductions in total LDL–C (~20%), a parameter known to be correlated with risk of cardiovascular disease and death. The onset of the LDL-C lowering was rapid with a maximal effect seen by two weeks of treatment which was stably retained up to the end of the 8 weeks of treatment. LDL-C levels returned to pre-treatment levels within two weeks after treatment was stopped.

In addition, adding treatment with atorvastatin to MBX-8025 increased the percent change in LDL-C by approximately an additional 20% compared to that of MBX-8025 dosed alone in those patients with baseline

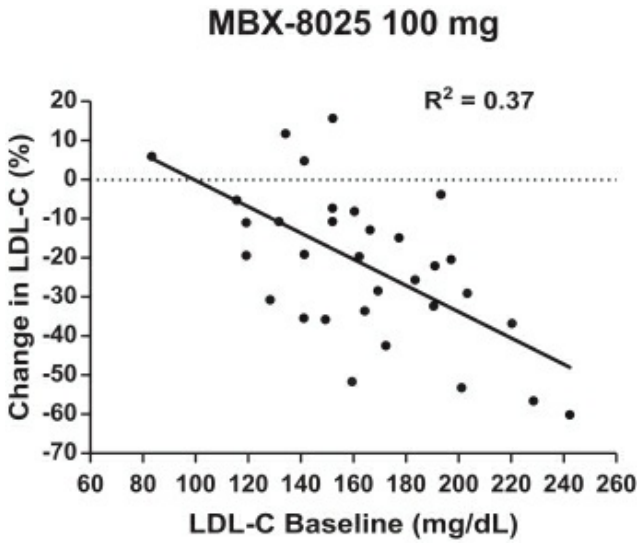
LDL-C ³ 175mg/dL. Decreases in LDL-C were correlated with baseline values, as shown in the figures below. Patients with higher baseline LDL-C values experienced larger reductions in LDL-C. Patients with baseline LDL-C in the 200 mg/dL range had reductions of approximately 40 to 50% with a dose response pattern between the 50 and the 100 mg doses. This suggests that higher doses of MBX-8025 (>100 mg) could potentially produce even larger decreases in LDL-C.

Change in LDL-C (%) according to baseline LDL-C



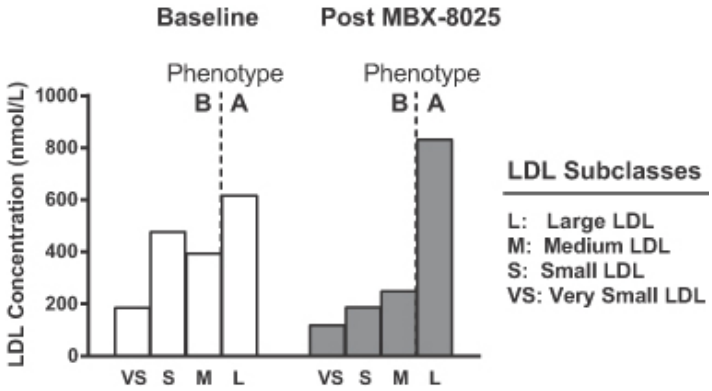
The correlation between baseline LDL-C levels and percentage change in LDL-C for subjects receiving 100 mg MBX-8025 is shown in the graph below and demonstrates a larger effect at higher baseline LDL-C values. These data suggest that MBX-8025 could potentially be a particularly effective treatment for diseases in which LDL-C is markedly elevated.

Individual Patient % Change from Baseline in LDL-C according to Baseline LDL-C



In this trial, lipoprotein particle size measurements were also performed to assess the effect of MBX-8025 on LDL particle subtype distribution. It is believed that small dense LDL particles (type B) are the more atherogenic subtype and that they confer a greater risk for atherogenesis (promotion of arterial plaque formation).

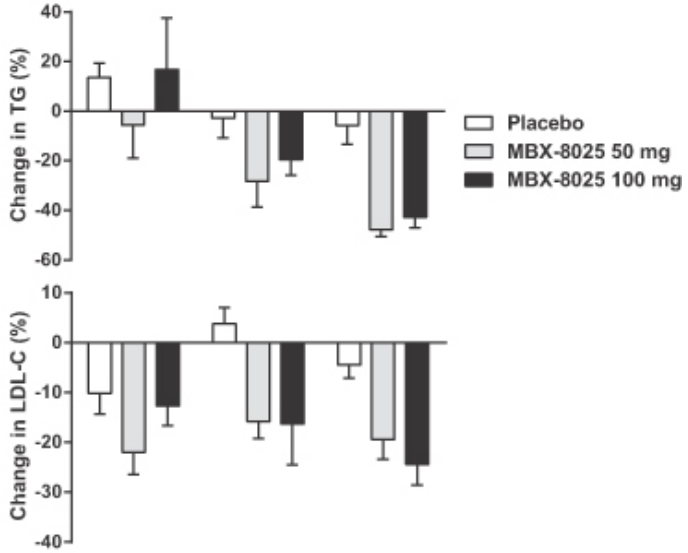
As shown below, MBX-8025 selectively depleted the small dense LDL particles, converting them to the larger, more buoyant and less atherogenic phenotype A.



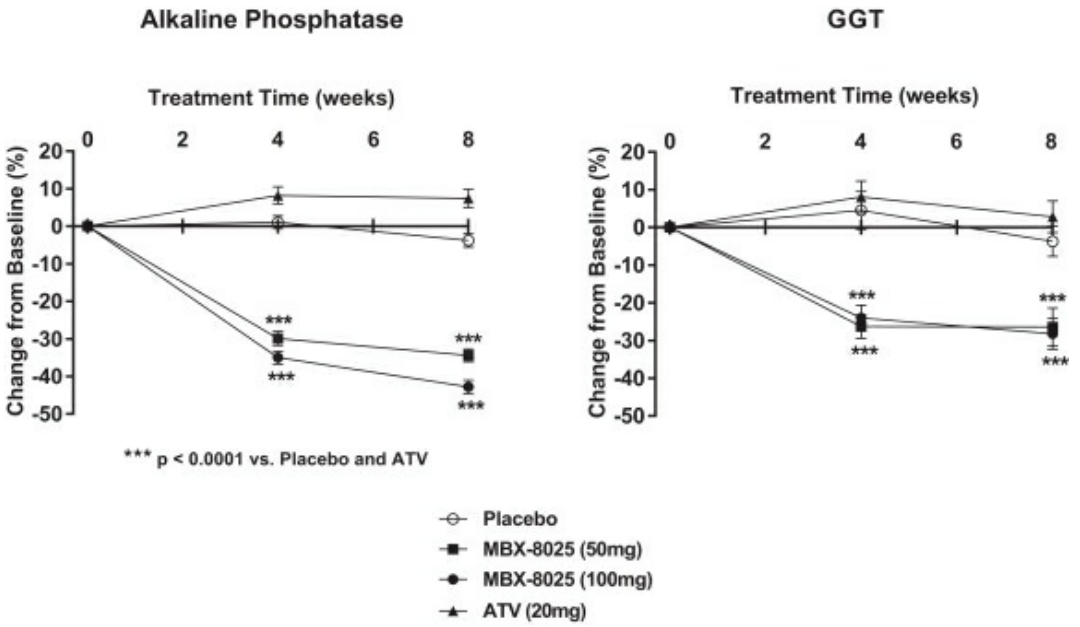
Another beneficial effect of MBX-8025 observed in this Phase 2 clinical trial was a decrease in both TGs (~30%) and free fatty acids (10-15%). The reductions in TGs are illustrated in the figure below where the effect is shown as a function of baseline TG concentration (subdivided into three groups as defined by the National Cholesterol Education Program Adult Treatment Panel III, or NCEP ATP III). At baseline values above 200 mg/dL, the reductions are approximately 50%. Also shown in this figure are the changes in LDL-C for the same patients that experienced the reductions in TGs. At all doses of MBX-8025, the reductions in TGs are associated with a concomitant reduction (15-25%) in LDL-C. Thus, MBX-8025 lowered both TGs and LDL-C in the same patients in this clinical trial. A similar pattern of simultaneous decreases in TGs and LDL-C were observed in the MBX-8025 plus atorvastatin arms of the trial.

Change in TG as a function of baseline TG by NCEP ATP III:

NCEP ATP III	Normal TG	Borderline TG	High TG
TG range	<150	150-199	≥ 200
Mean TG	119-133	171-187	264-295
N	2, 5, 3	10, 7, 6	14, 14, 23



MBX-8025 also produced statistically significant decreases in GGT and AP at both doses of 50 and 100 mg, whereas there were no changes with either placebo or atorvastatin. GGT has been described as a marker of liver inflammation that is associated with the deposition of fat in the liver and AP is a validated marker of liver cholestasis.



Future Development Plan for MBX-8025

We have decided to redirect the development of MBX-8025 toward serious rare and orphan diseases or more prevalent diseases with higher unmet medical need. We have focused on diseases in which there is a clear scientific rationale or clinical data to suggest that the beneficial effects of MBX-8025 observed in our mixed dyslipidemia trial may be retained in that disease population. The indications of interest are HoFH, SHTG, PBC and NASH.

Homozymogous Familial Hypercholesterolemia (HoFH)

HoFH is a rare, life-threatening, genetic disease characterized by marked elevations in plasma levels of LDL-C leading to severe atherosclerosis and the development of premature cardiovascular diseases. While normal LDL-C levels are approximately 100 mg/dL, patients with HoFH may have levels in the 500 to 1000 mg/dL range. Symptomatic cardiovascular disease often presents during the first decades of life leading to myocardial infarction, ischemic stroke, and death. If untreated, most HoFH patients do not survive beyond the age of 30.

HoFH is caused by loss-of-function mutations in both genes of the low-density lipoprotein receptor (LDL-R) protein, leading to reduced or absent LDL-R function. The disease affects approximately one in one million persons. The loss of LDL-R function leads to impaired removal by the liver of LDL-C from the circulation, resulting in exceptionally high LDL-C blood concentrations.

Treatment of HoFH is focused on reducing LDL-C levels, as compelling evidence exists from randomized, double-blind, placebo-controlled studies to support the causality of LDL-C in atherosclerotic cardiovascular disease. Considerable evidence implicates LDL-C as a causal mediator of cardiovascular disease in HoFH

patients and reductions in LDL-C can be expected to decrease the risk of cardiovascular disease. It is known that HoFH subjects undergoing LDL-C apheresis, have a reduction in cardiovascular disease events.

Initial treatment of HoFH entails adoption of a low fat diet and exercise program, usually with limited effectiveness. This is followed by conventional pharmacological therapies for reducing LDL-C, including statins, cholesterol absorption inhibitors and bile acid sequestrants. Unfortunately, these conventional therapies work largely through up-regulation of the LDL-R. Thus, they are minimally effective in patients with HoFH in whom LDL-R activity is impaired or absent. Patients having a small amount of residual LDL-R activity may receive a modest reduction in LDL-C with maximal conventional therapy, but most patients with HoFH respond insufficiently.

Plasma apheresis is a selective mechanical filtration of blood that may be used to remove LDL-C and is currently a treatment of choice for HoFH. However, apheresis is a complex and inconvenient procedure that could require an arterio-venous fistula and has numerous side effects. The procedure is not widely available throughout the US and Europe. Apheresis reduces LDL-C levels transiently, but must be repeated every one to two weeks because LDL-C levels rebound.

Two new drugs have recently been approved for use in combination with diet, exercise and conventional lipid lowering therapy to treat HoFH. The first is lomitapide (Juxtapid, Aegerion® Pharmaceuticals) that lowers LDL-C by inhibiting microsomal triglyceride transfer protein (MTP), a protein whose activity is required for the production of very low density lipoprotein (VLDL-C), a precursor of LDL-C. Lomitapide produces decreases in LDL-C of approximately 40% from a baseline LDL-C level of 337 mg/dL and gets 28% of patients to the LDL-C target of <100 mg/dL. A side effect of lomitapide treatment is that fat accumulates in the liver, thereby causing hepatic steatosis, with or without concurrent increases in transaminases. For this reason, the drug carries a black box warning and a requirement for monthly liver function monitoring tests. Lomitapide also blocks MTP in enterocytes (cells lining the gastrointestinal tract), leading to an accumulation of fat in the intestinal mucosa. This can reduce the absorption of fat-soluble nutrients and causes gastrointestinal issues (diarrhea, abdominal pain). Subjects on lomitapide should be prescribed concomitant fat-soluble vitamin supplementation and should adhere to a restrictive diet supplying less than 20% of energy from fat.

The second drug is mipomersen (Kynamro, ISIS Pharmaceuticals). It lowers LDL-C by acting as an anti-sense oligonucleotide inhibitor that blocks the synthesis of apo B-100, the protein component of LDL-C. Mipomersen lowers LDL-C by approximately 25% from a baseline LDL-C of 439 mg/dL. Like lomitapide, mipomersen causes the accumulation of fat in the liver, confers a risk of hepatic steatosis and carries a black box warning and requirement for monthly liver function monitoring tests.

While these two newly registered drugs offer additional treatment options for patients with HoFH, there remains a high degree of unmet medical need. Even with an aggressive combination of available therapies, subjects with HoFH generally have LDL-C levels substantially above treatment targets. Many patients also have difficulty accessing or tolerating available treatments. We believe that MBX-8025 has attributes that are well suited to the treatment of HoFH and should be independent of the LDL-R activity. This is supported by studies on another PPARd agonist, GW501516, in mice that lack the LDL-R. Thus, we hypothesize that the LDL-C lowering effect observed in our earlier studies in patients with mixed dyslipidemia may be transferable to patients with HoFH . If MBX-8025 is able to reduce LDL-C in these patients and retains the favorable safety profile observed thus far in our clinical studies, we believe it has the potential to be the front line pharmacological treatment for HoFH. We plan to conduct a small placebo-controlled double-blind proof-of-concept Phase 2 study in patients with HoFH to test this hypothesis.

It is likely that many patients with HoFH will require combination therapy with LDL-C lowering agents in order to achieve enough lowering of LDL-C to reach goal of < 100 mg/dL. Thus we believe there may be opportunities to combine MBX-8025 with other therapies including lomitapide or mipomersen. In this scenario, we note that the ability of MBX-8025 to reduce hepatic fat may potentially mitigate or prevent the development of hepatic steatosis and steato-hepatitis associated with lomitapide and mipomersen.

Severe Hypertriglyceridemia (SHTG)

Severe HTG (SHTG, TGs > 500 mg/dL) is associated with an increased risk of pancreatitis. As a result, management of HTG and SHTG is also an important goal of lipid therapy. Most patients with HTG can be managed with available TG-lowering therapies including fibrates, niacin and fish oil components. However, there remains an unmet need for addressing SHTG which may arise from a variety of circumstances. It is estimated that there are approximately five million patients in the US with SHTG; however, the Fredrickson classification of hyperlipidemias further subdivides the overall population into several types, some of which can be classified as orphan diseases.

According to the Fredrickson classification of hyperlipidemias, several types of HTG have been identified. This includes Type 1a, a rare genetic disease also called familial chylomicronemia syndrome (FCS), in which chylomicrons are markedly elevated due to decreased activity of liporprotein lipdase (LPL), the enzyme that is primarily responsible for their metabolism. FCS affects about one in one million people worldwide. Type 1b is another form characterized by a deficiency in a protein component of chylomicrons called apo-CII which is needed to activate LPL and facilitate chylomicron metabolism. Another form is Type 5 in which very low density lipoprotein (VLDL) is elevated in addition to chylomicrons and is likely caused by yet incompletely defined variety of molecular defects.

The need for better treatments for SHTG has been recognized and several new therapies either have been brought to the market or are in development. One popular approach has been to develop components of fish oil. Lovaza is a marketed drug that is a mixture of the omega-3 fatty acids esters eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) isolated from fish oil. In patients with SHTG (TGs > 500 mg/dL), it has been shown to reduce TGs by over 40%, but the reductions are accompanied by increases in LDL-C of over 40%. Vascepa, an ethyl ester of EPA, is also on the market for the treatment of SHTG and lowers TGs by approximately 30% with no significant effect on LDL-C. Epanova is a complex mixture of polyunsaturated free fatty acids derived from fish oils, including multiple long-chain omega-3 and omega-6 fatty acids, with EPA, DHA, and docosapentaenoic acid being the most abundant forms. In patients with SHTG, Epanova produced decreases in TGs of approximately 30% with increases of approximately 25% in LDL-C.

Other drugs are currently in earlier stage development for SHTG. ISIS-APOCIIIRX,is an oligonucleotide inhibitor of apo-CIII, a lipoprotein component that regulates TG metabolism. Loss-of-function mutations in apo-CIII are associated with lower levels of TGs. In a Phase 2 study in patients with SHTG, ISIS-APOCIIIRX produced reductions in TGs of up to 70%. The effects on LDL-C were not reported. Another product candidate, CAT-2003, produced decreases in both fasting and post prandial (post meal) TGs in normal healthy volunteers and has been advanced into Phase 2 studies in SHTG.

We believe that MBX-8025 may be uniquely able to benefit patients with SHTG by virtue of its ability to simultaneously lower TGs and LDL-C. This benefit has been observed both in monotherapy as well as in combination with atorvastatin in patients with mixed dyslipidemia. Drugs currently marketed for the treatment of SHTG lower TGs with either a worsening or lack of meaningful improvement in LDL-C. Recognizing that SHTG is a heterogeneous collection of diseases, we are continuing our assessment of the best patient populations to study in a small Phase 2 clinical trial.

Primary Biliary Cirrhosis (PBC)

PBC is a slowly progressive autoimmune disease of the liver characterized by portal inflammation and immune-mediated destruction of intrahepatic bile ducts. The loss of bile duct function leads to decreased bile secretion and the retention of toxic substances within the liver, resulting in further hepatic damage, fibrosis, cirrhosis and, eventually, liver failure. It is a common cause of liver transplantation.

PBC affects primarily women with peak incidence in the fifth decade of life. It has been recognized as an orphan disease both in the US and in the EU. It is a long-term debilitating and life-threatening disease. Fatigue

and pruritus are the most common presenting symptoms. Pruritus (itching), which occurs in 20 to 70% of patients, can be extremely distressing for patients. Other common findings include jaundice, hyperlipidemia (notably hypercholesterolemia), hypothyroidism, osteopenia and osteoporosis, and coexisting autoimmune diseases. Portal hypertension is a late complication of the disease, as is malabsorption, deficiencies of fat-soluble vitamins, and steatorrhea (excess fat in feces).

Currently, the only FDA-approved treatment is ursodeoxycholic acid, also known as ursodiol, an isomer of chenodeoxycholic acid. Ursodiol decreases serum levels of AP, bilirubin, alanine aminotransferase, aspartate aminotransferase, cholesterol, and immunoglobulin M, all of which are elevated in patients with PBC and can serve as biochemical markers of the disease. In a study that combined data from three controlled trials with a total of 548 patients, ursodiol significantly reduced the likelihood of liver transplantation or death after four years. Ursodiol also delayed the progression of hepatic fibrosis in early-stage PBC, but was not effective in advanced disease. It is also known that up to 50% of PBC patients fail to respond to ursodiol therapy.

Other therapies, such as colchicine, methothrexate, prednisone and multiple immunosuppressive regimens have been attempted. However, their efficacy is controversial, limited, or unproven and they are associated with multiple side-effects impacting tolerance and safety. Liver transplantation improves survival in patients with PBC, and it is the only effective treatment for those with liver failure. However cirrhosis recurs in 15% of patients at three years and in 30% at 10 years. As a result, despite the previously mentioned therapeutic interventions, it is recognized that PBC continues to progress in many patients and additional medical treatment is needed to address this disease.

The bile acid analog obeticholic acid (OCA) is in development (Intercept Pharmaceuticals) for PBC. OCA has received orphan designations in US and EU and Fast Track status in the US. Clinical proof-of-concept has been established in two 12-week Phase 2 studies (one in ursodiol non-responders and one in treatment naïve or intolerant patients) using AP as the primary endpoint (<1.67 times the upper limit of normal with >15% reduction) + normal bilirubin. Approximately 40% of patients met the primary endpoint. A Phase 3 study has recently been completed that met its primary endpoint. It remains unclear what the criteria are for registration.

Both AP and GGT are common biochemical markers of cholestasis and their elevation is presumably a consequence of the toxic effects of retention of bile acids in cells in the biliary duct. AP levels in PBC patients have been used as a primary outcome measure in proof-of-concept clinical trials and as a key secondary outcome in pivotal trials. The observation that MBX-8025 produces significant reductions in these surrogate markers suggests that the drug may improve biliary function, ameliorate cholestasis and, hence, be a novel treatment for PBC. The coordinate decrease in AP and GGT levels indicates that the AP decrease is indeed hepatic in origin. The magnitude of the change in AP with MBX-8025 (~40%) is similar to that seen after treatment with ursodeoxycholic acid after eight weeks. In addition to the potential benefit to improving biliary function, we believe MBX-8025 may confer improvements in lipid parameters including reductions in LDL-C and TGs.

The precise mechanism by which MBX-8025 improves cholestasis by acting as a PPARd agonist is not fully understood. However, there is some supporting preclinical data. In the bile ligation model of cholestasis, the PPARd agonist KD3010 reduced hepatic injury, fibrosis and inflammation, while increasing survival. In addition, treatment of mice with the PPARd agonist GW610742 has been shown to produce significant and large increases in bile flow and the production of bile salts.

We are currently evaluating the initiation of a Phase 2 proof-of-concept study for MBX-8025 in patients with PBC.

Non-Alcoholic Fatty Liver Disease (NAFLD) / Nonalcoholic Steatohepatitis (NASH)

NAFLD is a disease characterized by accumulation of fat in the liver of people who drink little or not at all. Approximately one-third of NAFLD patients develop NASH, which is characterized by inflammation in the liver

that is often accompanied by fibrosis. This can progress to cirrhosis, followed by eventual liver failure and death. NASH is the third most common reason for liver transplantation in the United States. NASH is a major challenge to healthcare systems worldwide. NASH is initially a silent disease, the first sign of which may be elevations in transaminases such as alanine aminotransferase (ALT) or aspartate aminotransferase (AST) from routine blood test panels. When further evaluation rules out medications, viral hepatitis, alcohol, etc. as a cause, or when imaging studies of the liver show fat, NASH is suspected. A confirmation of a diagnosis of NASH requires a liver biopsy.

There are currently no drugs approved by the FDA for the treatment of NASH. However, a number of clinical studies have been carried out or are underway with drug candidates that may affect disease outcomes in patients with NASH, including OCA (Intercept Pharmaceuticals) and GFT505, a PPARa/d agonist (Genfit).

Based on data from our Phase 2 clinical trial in patients with mixed dyslipidemia and available data from other PPARd agonists, we believe MBX-8025 may have utility in treating patients with NASH. The decrease in GGT, a biochemical marker which has been recognized to be linked with hepatic fat accumulation, observed in our phase 2 mixed dyslipidemia trial is consistent with results reported for another PPARd agonist GW501516. A short term clinical trial with GW501516 investigators demonstrated that the compound decreased hepatic fat. In addition to our clinical experience with MBX-8025, along with that of other PPARd agonists, the well documented property that MBX-8025 induces the oxidation of fatty acid leads us to believe that our compound could potentially benefit patients affected with NAFLD who are further at risk of developing NASH. Although we do not currently anticipate near term development of MBX-8025 in NASH, we continue to evaluate the opportunity among a number of additional indications.

Cymabay Clinical Strategy for MBX-8025

Our initial strategy is to evaluate and carry out pilot or proof-of-concept clinical trials in HoFH, SHTG and PBC to assess whether MBX-8025 is able to produce the predicted improvements in the relevant biomarkers associated with these diseases. In all three indications, clinically and statistically significant markers of disease status can be achieved in relatively small (10-20 patients) studies of three months or less duration. In cases where clinical proof-of-concept is achieved, we believe that we could move rapidly into a Phase 3 registration program based on the high unmet need in these indications. We continue to assess a variety of criteria (patient availability, regulatory pathway clarity, commercial attractiveness, etc.) with which to prioritize these indications. We plan to initiate one or more pilot or proof-of-concept studies for MBX-8025, beginning with HoFH, in the first half of 2015.

MBX-2982

Type 2 diabetes is a chronic debilitating disease characterized by a progressive loss of the normal control of glucose levels in the blood and other tissues. There are several established and emerging classes of drug therapies for diabetes. Over the last decade, injectable drugs have emerged as competing drugs with significant benefits in glucose control as well as effects on weight loss and the potential to protect the pancreas from the damage caused by the progression of diabetes. These drugs are primarily analogs of the natural hormone glucagon-like 1 peptide (GLP-1), and include exenatide, liraglitide and lixisenatide among others. These drugs are given by subcutaneous injection once or twice daily. Their action is to provide glucose-regulated insulin secretion with weight loss and the potential to preserve function of pancreatic islets. New members of this class with once weekly to once monthly dose schedules have been approved or are in late stage development. In spite of the variety of drugs available for the treatment of diabetes, the medications used to manage diabetes have not led to optimal control of hyperglycemia and many are associated with dose-limiting side effects. MBX-2982 is an oral, G-protein coupled receptor (GPR119) agonist being evaluated as a novel therapeutic agent for patients with T2DM, with a dual mechanism including direct effects and indirect effects mediated by gastrointestinal hormones known as incretins on glucose-dependent insulin secretion, as well as potentially beneficial effects on islet health.

GPR119 is expressed in pancreatic islet cells and gastrointestinal hormone secreting cells (enteroendocrine cells). Activation of GPR119 in pancreatic ß-islets either by natural (endogenous) substances or by drugs developed to interact with it (GPR119 agonists) results in direct stimulation of glucose-dependent insulin secretion *in vitro*. Activation of GPR119 in intestinal enteroendocrine cells either by endogenous substances or by GPR119 agonists results in stimulation of glucagon-like peptide 1 (GLP-1) and gastrointestinal inhibitory peptide release, and subsequent enhanced glucose-dependent insulin secretion and suppression of glucagon, leading to improved acute glucose tolerance, both *in vitro* and *in vivo*. MBX-2982 was synthesized and screened as a GPR119 agonist, and is capable of activating endogenous GPR119 in a cell line over-expressing the receptor. MBX-2982 has been shown to increase glucose-dependent insulin secretion in both *in vitro* and in animal models. MBX-2982 also increases incretin hormone levels in animals, which may contribute to its glucose lowering effects.

Nonclinical studies show that MBX-2982 has desirable effects on blood glucose levels, and this effect is additive to the effect of the dipeptidyl peptidase-4 (DPP-4) inhibitor, sitagliptin. Based on these results, there may be an important role for MBX-2982 as a novel therapeutic agent in the treatment of T2DM, alone or in combination with other anti-diabetic agents, including the DPP-4 inhibitors. Presently, there are no other agents approved in the U.S. within this pharmacologic class for the treatment of T2DM.

Extensive preclinical toxicological (up to 6 months in rats and dogs) have been completed, and PK profiling of MBX-2982 has shown low potential for safety risk. We filed an IND for MBX-2982 with the FDA in January 2008.

Clinical Studies with MBX-2982

Four Phase 1 clinical studies and one Phase 2 clinical study with MBX-2982 have been completed and the safety and PK review showed no safety or tolerability concerns with MBX-2982 administered in escalating doses (25, 100, and 300 mg/day) tested for up to 4 weeks of dosing. A four-week study in type 2 diabetics can be summarized as follows:

- MBX-2982 generally lowered mean weighted glucose and post-meal glucose during an extended mixed-meal tolerance test (MMTT), although not always to a statistically significant degree and not to the extent of sitagliptin. The effect at the 300 mg dose may have been mitigated by the inclusion of a very small number of patients who experienced extreme worsening of glucose to the degree of being statistical outliers. Decreases in fasting glucose were generally not observed with MBX-2982.
- Four weeks of treatment with MBX-2982 tended to increase insulin, active GLP-1, and total GLP-1 during an extended MMTT. Decreases in glucagon were not as consistently observed. Changes in active GLP-1 were not as robust as those observed with sitagliptin. Four weeks of treatment with MBX-2982 also tended to increase fasting insulin and c-peptide, and decrease fasting triglycerides.
- Overall, the data suggest that MBX-2982 may decrease glucose, potentially through effects on GLP-1, glucagon, and insulin. Changes in HbA1c are difficult to assess over a 4-week treatment period, but trended in the downward direction. Glucose-lowering effects and mechanism of action will need to be explored more robustly in longer duration trials of MBX-2982.
- The PK results observed in this study are similar to those seen in the completed Phase 1 study that used the same formulation, demonstrating dose-dependent increases in drug exposure and a profile supporting once daily oral dosing.
- MBX-2982 at doses of 25, 100, and 300 mg was safe and well tolerated.

Based on these results, we believe further testing with MBX-2982 in combination with sitagliptin and/or metformin for the treatment of diabetes is warranted.

Next Steps in Development of MBX-2982

Prior to conducting the fourth Phase 1 clinical study and the Phase 2 clinical study, we entered into an exclusive license agreement for MBX-2982 with Sanofi-Aventis in June 2010. In June 2011, Sanofi-Aventis terminated the license and has no further rights to MBX-2982. A proof-of-concept study has been designed to determine the effects of MBX-2982 on fasting and post-challenge blood glucose in patients with T2DM either as dual therapy in combination with either metformin or sitagliptin, or as triple therapy in combination with metformin and sitagliptin. Successful achievement of study goals would position the drug for a Phase 2b study, followed by a Phase 3 program.

We do not anticipate conducting this study until a suitable partner is found to contribute funding or resources for the project, or until sometime in the future when we have sufficient capital resources.

License Agreements and Intellectual Property

General

CymaBay actively seeks to obtain, where appropriate, patent protection and regulatory exclusivity for the proprietary technology that it considers important to its business, including compounds, compositions and formulations, their methods of use and processes for their manufacture both in the United States and other countries. CymaBay also relies on trade secrets, know-how, continuing technological innovation and in-licensing to develop and maintain its proprietary position. Our success depends in part on our ability to obtain, maintain and enforce proprietary protection for our product candidates, technology and know–how, to operate without infringing the proprietary rights of others, and to exclude others from infringing our proprietary rights. However, patent protection may not afford CymaBay complete protection against competitors who seek to circumvent CymaBay's patents.

CymaBay also depends upon the skills, knowledge, experience and know-how of its management, research and development personnel, as well as that of its advisors, consultants and other contractors. To help protect its proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, CymaBay currently relies and will in the future rely on trade secret protection and confidentiality agreements to protect its interests. To this end, CymaBay requires all of its employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to it of the ideas, developments, discoveries and inventions important to its business.

Collaborations and Licensing Agreements

CymaBay has entered into various arrangements with licensors and licensees. The current collaborations are summarized below.

Johnson and Johnson: In August 2006, CymaBay entered into a strategic alliance with Ortho-McNeil, Inc. As part of the alliance, Janssen Pharmaceutical NV, an affiliate of Ortho-McNeil, granted to CymaBay an exclusive worldwide, royalty-bearing license to MBX-8025 and certain other PPARd compounds (the "PPARd Products") with the right to grant sublicenses to third parties to make, use and sell such PPARd Products. Under the terms of the agreement, CymaBay has full control and responsibility over the research, development and registration of any PPARd Products and is required to use diligent efforts to conduct all such activities. Janssen has the sole responsibility for the preparation, filing, prosecution, maintenance of, and defense of the patents with respect to, the PPARd Products. Janssen has a right of first negotiation under the agreement to license a particular PPARd Product from CymaBay in the event that CymaBay elects to seek a third party corporate partner for the research, development, promotion, and/or commercialization of such PPARd Products. Under the terms of the agreement Janssen is entitled to receive up to an 8% royalty on net sales of PPARd Products. Under the terms of the agreement, if CymaBay does not expend more than a de minimus amount of effort and resources on the

research and/or development of at least one PPARd product, such action would constitute a default under the agreement. In addition, if CymaBay fails to make any payment called for under the agreement, discloses any non-exempt confidential information related to the agreement, or fails to use diligent efforts to promote, market and sell any PPARd product under the agreement, such action would constitute a default under the agreement. In the event of such default, or upon CymaBay's termination of the agreement, CymaBay shall grant Janssen a worldwide, exclusive, irrevocable license under the agreement in all information that is controlled, developed or acquired by CymaBay which relate to a PPARd compound or PPARd product and in all patents that are filed during the term of the agreement with a priority date after the effective date of the agreement and relate to a PPARd compound or PPARd product.

In June 2010, CymaBay entered into two development and license agreements with Janssen Pharmaceuticals, Inc. (Janssen) to further develop and discover undisclosed metabolic disease target agonists for the treatment of T2DM and other disorders and received a one-time nonrefundable technology access fee related to the agreements. CymaBay is also eligible to receive up to $228 million in contingent payments if certain development and commercial events are achieved as well as royalties on worldwide net sales of products. No such payments have been made to date. Under the terms of the agreements, Janssen has full control and responsibility over the research, development and registration of any products developed and/or discovered from the metabolic disease targets and is required to use diligent efforts to conduct all such activities. A joint steering committee with equal representation from each party will oversee the development of products. Following June 2012, all decisions of the joint steering committee will be made by Janssen. CymaBay has the sole responsibility, for the preparation, filing, prosecution, maintenance of, and defense of the CymaBay patents with respect to, metabolic disease target agonists. Under the terms of the agreements, if CymaBay discloses any non-exempt confidential information related to the agreements, such action would constitute a default under the agreements. In addition, if CymaBay breaches any of its representations or warranties under the agreements, such action would constitute a default. In the event of a default, the agreements do not provide that CymaBay will lose any of its rights to the intellectual property developed under the agreement.

DiaTex: On June 30, 1998, we entered into a License and Development Agreement with DiaTex, Inc. Under the agreement, DiaTex granted us an exclusive license to develop and commercialize therapeutic products containing halofenate, its enantiomers (mirror images, including arhalofenate), derivatives, and analogs (the licensed products) for the treatment of diseases. Under terms of the agreement, DiaTex will work cooperatively and assist us in conducting a program for the research and development of halofenate and its enantiomers including the right to sublicense, to use and to practice all patents controlled by DiaTex that claim halofenate and its enantiomers, and all information, data, know-how, trade secrets, inventions, developments, results, techniques and materials, whether or not patentable, that are necessary or useful towards such commercialization. Under the agreement, we are obligated to use diligent efforts to conduct preclinical and clinical testing of halofenate and its enantiomers in order to determine its efficacy for use in the treatment or prevention of human diseases or conditions. On April 15, 1999 the agreement was amended by the parties to allow DiaTex to transfer to us their interest in an IND application that they filed with the FDA. The amendment also provided for DiaTex to indemnify us against any and all losses resulting or arising from any third party claims, actions or proceedings under the IND application, any negligent or wrongful acts or omissions of DiaTex in connection with the IND application, and any misrepresentations by DiaTex relating to the license agreement. Under the amendment, we will provide the same indemnifications to DiaTex with respect to any third party claims, actions, or proceedings in connection with negligent or wrongful conduct of clinical trials relating to the license agreement, provided the claims are not related to negligent or wrongful acts or omissions committed by DiaTex.

The license agreement contains a $2,000 per month license fee as well as a requirement to make additional payments for development achievements and royalty payments on any sales of licensed products. DiaTex is entitled to up to $0.8 million for the future development of arhalofenate, as well as a 2% royalty payment on any net sales of products containing arhalofenate. A $50,000 milestone payment was made in May 2005 but no other milestone or royalty payments have been made since then. The agreement will expire upon the expiration of the last of DiaTex's patents related to the license granted, or, if later, the expiration of all payment obligations under

the agreement. The agreement may also terminate upon a material breach by DiaTex or us, if written notice of such breach is delivered to the breaching party, and the breaching party has not (i) cured the breach or (ii) initiated good faith efforts to cure the breach within a specified time period. Under the terms of the agreement, if we fail to use diligent efforts to conduct preclinical and clinical testing of halofenate and its enantiomers to determine its efficacy for use in the treatment or prevention of human diseases or conditions, fail to make any payment called for under the agreement, or disclose non-exempt confidential information under the agreement, such action would constitute a material breach under the agreement. In addition, if we fail to execute all instruments and assignments or fail to take any action to effect joint ownership of any enantiomer patent with DiaTex, such action would constitute a material breach under the agreement. We may terminate the agreement at any time if we determine we are no longer interested in DiaTex's license grant, provided we provide sufficient written notice within a specified time period.

Research and Development Agreements

INC Research: In February 2014, we entered into a Master Services Agreement with INC Research, LLC and related initial work order for INC Research to provide contract clinical research and development services to us in connection with our Phase 2b study. The Agreement provides that we may engage INC Research from time to time to provide services in accordance with work orders mutually agreed and budgeted between the parties for clinical research and development of arhalofenate which total is anticipated to exceed approximately $8 million. The master services agreement provides customary terms and conditions, including those for performance of services by INC Research in compliance with work orders, standard operating procedures, FDA and ICH requirements and all applicable laws. We remain responsible for all regulatory responsibilities and the determination of any work orders, subject to mutual agreement on the specific terms of any such work orders. The master services agreement has a term of five years; provided that we may terminate the master services agreement or any individual work order on thirty (30) days written notice, or immediately in the event of any safety risk associated with the services the being performed. In addition, either party may terminate the master services agreement or any applicable work order upon thirty (30) days written notice for a material breach by the other party.

Intellectual Property

CymaBay owns and co-owns approximately 31 United States patents, 179 foreign patents, as well as 26 United States patent applications and 190 foreign and Patent Cooperation Treaty applications which are counterparts to certain United States patents and patent applications. In addition, we license from third parties approximately 17 United States patents and 1 United States patent application, 222 foreign patents and 68 foreign and Patent Cooperation Treaty applications which are counterparts to certain United States patents and patent applications. These patents and patent applications include claims covering various aspects of our product pipeline and research and development strategies, including: arhalofenate crystal forms, methods of use both alone and in combination with other drugs and methods of manufacture, certain PPAR delta agonists, their compositions and uses, certain GPR119 agonist compositions and uses and undisclosed metabolic disease target agonist compositions and uses.

The arhalofenate portfolio consists of approximately 129 issued patents and 93 pending patent applications relating to composition, method of use or methods of manufacture. We believe our issued patents protect Arhalofenate through at least 2019-2029 before accounting for any potential patent term extension. The MBX-8025 portfolio consists of approximately 240 issued patents and 89 pending patent applications related to composition and method of use that we believe protect it through at least 2024-2026 before accounting for any potential patent term extension. Patent and trade secret protection is critical to our business. Our success will depend in large part on our ability to obtain, maintain, defend and enforce patents and other intellectual property to extend the life of patents covering our product candidates, to preserve trade secrets and proprietary know-how, and to operate without infringing the patents and proprietary rights of third parties we actively seek patent protection in the U.S.

Manufacturing

CymaBay does not currently own or operate manufacturing facilities for the production or testing of arhalofenate or other product candidates that it develops, nor does it have plans to develop its own manufacturing operations in the foreseeable future. CymaBay presently depends on third party contract manufacturers to obtain all of its required raw materials, Active Pharmaceutical Ingredients (APIs) and finished products for its clinical studies for arhalofenate. CymaBay has executed manufacturing agreements for its API and tablet supplies of arhalofenate with established manufacturing firms which are responsible for sourcing and obtaining the raw materials necessary for the finished products. The raw materials necessary to manufacture the API for arhalofenate, MBX-8025 and MBX-2982 are available from more than one source and CymaBay has also executed manufacturing agreements for the production of MBX-8025 and MBX-2982.

Siegfried AG

On April 30, 2012, CymaBay entered into a Development and Clinical Manufacture Agreement with Siegfried AG for the manufacturing of the API necessary for the tablet form of arhalofenate. Under the agreement, CymaBay shall deliver or Siegfried shall obtain the raw materials necessary for the API. CymaBay owns the rights, title and interest to the deliverables and intellectual property covering the deliverables generated under the agreement. Siegfried shall grant a non-exclusive license to CymaBay to use Siegfried intellectual property to exploit any product or service based or derived from the deliverables under the agreement. Both Siegfried and CymaBay have agreed to indemnify the other party with respect to losses due to the breach of a covenant or obligation under the agreement or the gross negligence, recklessness or intentional misconduct of the other party. CymaBay may terminate the agreement at any time with written notice and Siegfried may terminate the agreement in the event CymaBay discontinues its activities related to the development or commercialization of the API for arhalofenate. In addition, either party may terminate the agreement at any time for material breach under the agreement or in the case of insolvency of the other party.

Patheon Inc.

On June 5, 2012, CymaBay entered into a Development and Clinical Manufacture Agreement with Patheon Inc. for the manufacturing of the tablet form of arhalofenate. Under the agreement, CymaBay shall deliver the API or Patheon shall obtain the API from a qualified vendor. CymaBay owns the rights, title and interest to the deliverables and intellectual property generated by Patheon in connection with the performance of the services for CymaBay under the agreement. Both Patheon and CymaBay have agreed to indemnify the other party with respect to losses due to the breach of a covenant or obligation under the agreement or the gross negligence, recklessness or intentional misconduct of the other party. CymaBay may terminate the agreement at any time with written notice provided that CymaBay terminates the agreement within certain times in advance of the start date of certain services. In addition, either party may terminate the agreement at any time for material breach under the agreement.

Metrics Inc.

On October 31, 2006, CymaBay entered into a Standard Development Agreement with Metrics, Inc. Under the agreement, Metrics will provide CymaBay with pharmaceutical development, formulation and analytical services in consideration of which CymaBay will provide appropriate compensation as outlined in the agreement. CymaBay owns the rights, title and interest to the intellectual property relating to all pharmaceutical products developed or manufactured for CymaBay by Metrics, as well as any active pharmaceutical ingredient provided to Metrics by CymaBay. CymaBay has agreed to indemnify Metrics against third party claims that involve the breach by CymaBay of any of its obligations, warranties or representations under the agreement, and Metrics has agreed to indemnify CymaBay against third party claims that involve (i) the negligence, gross negligence, or intentional misconduct on the part of Metrics, (ii) a failure by Metrics to comply with the law in their performance of the agreement, or (iii) a breach of Metrics' obligations, covenants, representations, or warranties under the agreement. Either party may terminate the agreement at any time with advance written notice.

Research & Development Costs

Research and development costs for the years ended December 31, 2013 and 2012 were $4.5 million and $9.3 million, respectively, and were $6.7 million for the six months ended June 30, 2014.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those CymaBay is developing. The pharmaceutical drug product candidates that CymaBay develops must be approved by the Food and Drug Administration (FDA) before they may be legally marketed in the United States.

United States Pharmaceutical Product Development Process

In the United States, the FDA regulates pharmaceutical products under the Federal Food, Drug and Cosmetic Act, and implementing regulations. Pharmaceutical products are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on CymaBay. The process required by the FDA before a non-biological pharmaceutical product may be marketed in the United States generally involves the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices (GLP) or other applicable regulations;
- Submission to the FDA of an Investigational New Drug application (IND), which must become effective before human clinical studies may begin;
- Performance of adequate and well-controlled human clinical studies according to the FDA's current Good Clinical Practices (GCP), to establish the safety and efficacy of the proposed pharmaceutical product for its intended use;
- Submission to the FDA of a New Drug Application (NDA) for a new pharmaceutical product;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the pharmaceutical product is produced to assess compliance with the FDA's current Good Manufacturing Practice standards (cGMP), to assure that the facilities, methods and controls are adequate to preserve the pharmaceutical product's identity, strength, quality and purity;
- Potential FDA audit of the preclinical and clinical study sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the pharmaceutical product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product

chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the pharmaceutical product candidate. These early proof-of-principle studies are done using sound scientific procedures and thorough documentation. The conduct of the single and repeat dose toxicology and toxicokinetic studies in animals must comply with federal regulations and requirements including Good Laboratory Practices. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA has concerns and notifies the sponsor. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. If resolution cannot be reached within the 30-day review period, either the FDA places the IND on clinical hold or the sponsor withdraws the application. The FDA may also impose clinical holds on a pharmaceutical product candidate at any time before or during clinical studies due to safety concerns or non-compliance. Accordingly, CymaBay cannot be sure that submission of an IND will result in the FDA allowing clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate such clinical study.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the End-of-Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug.

Clinical studies involve the administration of the pharmaceutical product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the clinical study sponsor's control. Clinical studies are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, how the results will be analyzed and presented and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical studies must be conducted in accordance with GCP. Further, each clinical study must be reviewed and approved by an independent institutional review board (IRB) at, or servicing, each institution at which the clinical study will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical studies are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical study subject or his or her legal representative and must monitor the clinical study until completed.

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

- Phase 1. The pharmaceutical product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion.
- Phase 2. The pharmaceutical product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases, to determine dosage tolerance, optimal dosage and dosing schedule and to identify patient populations with specific characteristics where the pharmaceutical product may be more effective.
- Phase 3. Clinical studies are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical studies are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. The studies must be well-controlled and usually include a control arm for comparison. One or two Phase 3 studies are required by the FDA for an NDA approval, depending on the disease severity and other available treatment options.

- Post-approval studies, or Phase 4 clinical studies, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.
- Progress reports detailing the results of the clinical studies must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical studies may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical study at any time on various grounds, 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 study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the pharmaceutical product has been associated with unexpected serious harm to patients.

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

United States Review and Approval Processes

The results of product development, preclinical studies and clinical studies, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the pharmaceutical product, 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 substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act (PREA), an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the pharmaceutical product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any pharmaceutical product for an indication for which orphan designation has been granted.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act (PDUFA), the FDA has 10 months from filing in which to complete its initial review of a standard NDA and respond to the applicant, and six months from filing for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

After the NDA submission is accepted for filing, the FDA reviews the NDA application to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength,

quality and purity. The FDA may refer applications for novel pharmaceutical products or pharmaceutical products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the pharmaceutical product approval process, the FDA also will determine whether a risk evaluation and mitigation strategy (REMS) is necessary to assure the safe use of the pharmaceutical product. If the FDA concludes that a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without a REMS, if required.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites as well as the site where the pharmaceutical product is manufactured to assure compliance with GCP and cGMP. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. In addition, the FDA will require the review and approval of product labeling.

The NDA review and approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical studies are not always conclusive and the FDA may interpret data differently than CymaBay interprets the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical studies. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require Phase 4 testing which involves clinical studies designed to further assess pharmaceutical product safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Post-Approval Requirements

Any pharmaceutical products for which CymaBay receives FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, prohibitions on promoting pharmaceutical products for uses or in patient populations that are not described in the pharmaceutical product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, actions by the United States Department of Justice and/or United States Department of Health and Human Services Office of Inspector General, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available pharmaceutical products for off-label uses, manufacturers may not directly or indirectly market or promote such off-label uses.

CymaBay relies, and expects to continue to rely, on third parties for the production of clinical and commercial quantities of CymaBay's products. Manufacturers of CymaBay's products are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. cGMP regulations require, among other things, quality control and quality assurance, as well as the corresponding maintenance of records and documentation. Pharmaceutical product manufacturers and other entities involved in the manufacture and distribution of approved pharmaceutical products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

The FDA also may require post-marketing testing, known as Phase 4 testing, risk minimization action plans and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, or FCPA, prohibits certain individuals and entities, including CymaBay, from promising, paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, directly or indirectly, to obtain or retain business or an improper advantage. The U.S. Department of Justice and the U.S. Securities and Exchange Commission, or SEC, have increased their enforcement efforts with respect to the FCPA. Violations of the FCPA may result in large civil and criminal penalties and could result in an adverse effect on a company's reputation, operations, and financial condition. A company may also face collateral consequences such as debarment and the loss of export privileges.

Federal and state fraud and abuse laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain business practices in the biopharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease, or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and CymaBay's practices may not in all cases meet all of the criteria for statutory exemptions or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The reach of the Anti-Kickback Statute was also broadened by the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute. Pursuant to the statutory amendment, a person or entity no longer needs to have

actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses. Many states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act, which state laws apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Also, the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payers and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Because of the breadth of these laws and the narrowness of the federal Anti-Kickback Statute's safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Such a challenge could have a material adverse effect on our business, financial condition and results of operations. If CymaBay obtains FDA approval for any of our product candidates and begin commercializing those products in the United States, CymaBay's operations may be directly, or indirectly through our customers, distributors, or other business partners, subject to various federal and state fraud and abuse laws, including, without limitation, anti-kickback statutes and false claims statutes. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates"—independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

If CymaBay's operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to CymaBay, CymaBay may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs, and the curtailment or restructuring of CymaBay's operations, any of which could adversely affect CymaBay's ability to operate its business and CymaBay's results of operations. To the extent that any of CymaBay's product candidates are ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of CymaBay's pharmaceutical product candidates, some of CymaBay's patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments 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 pharmaceutical product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, CymaBay may intend to apply for restoration of patent term for one of its currently owned or licensed patents to add patent life beyond its current expiration date, depending upon the expected length of the clinical studies and other factors involved in the filing of the relevant NDA.

Market exclusivity provisions under the U.S. Food, Drug, and Cosmetic Act can also delay the submission or the approval of certain applications of other companies seeking to reference another company's NDA. Currently seven years of reference product exclusivity are available to pharmaceutical products designated as Orphan Drugs, during which the FDA may not approve generic products relying upon the reference product's data. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric clinical study in accordance with an FDA-issued "Written Request" for such a clinical study.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical product candidates for which CymaBay obtains regulatory approval. In the United States and markets in other countries, sales of any products for which CymaBay receives regulatory approval for commercial sale will depend in part upon the availability of reimbursement from third-party payors. Third-party payors include government payors such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a pharmaceutical product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the pharmaceutical product. Third-party payors may limit coverage to specific pharmaceutical products on an approved list, or formulary, which might not include all of the FDA-approved pharmaceutical products for a particular indication.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. CymaBay may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of its products, in addition to the costs required to obtain the FDA approvals. CymaBay's pharmaceutical product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a pharmaceutical product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable CymaBay to maintain price levels sufficient to realize an appropriate return on CymaBay's investment in product development. In addition, in the United States there is a growing emphasis on comparative effectiveness research, both by private payors and by government agencies. To the extent other drugs or therapies are found to be more effective than CymaBay's products, payors may elect to cover such therapies in lieu of CymaBay's products and/or reimburse CymaBay's products at a lower rate.

In 2003, the United States government enacted legislation providing a partial prescription drug benefit for Medicare recipients, which became effective at the beginning of 2006. Government payment for some of the costs of prescription drugs may increase demand for any products for which CymaBay receives marketing approval. However, to obtain payments under this program, CymaBay would be required to sell products to Medicare recipients through prescription drug plans operating pursuant to this legislation. As part of their participation in the Medicare prescription drug program, these plans negotiate discounted prices for prescription drugs and will likely do so for CymaBay's products. Federal, state and local governments in the United States continue to consider legislation to limit the growth of health care costs, including the cost of prescription drugs. Future legislation and regulations could limit payments for pharmaceuticals such as the drug candidates that CymaBay is developing.

Different pricing and reimbursement schemes exist in other countries. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any pharmaceutical product candidates for which CymaBay receives regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and CymaBay expects this will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which CymaBay receives regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. 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 Part A and B, Part D coverage is not standardized. 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. 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 CymaBay's products for which CymaBay receives marketing approval. However, any negotiated prices for CymaBay's products covered by a Part D prescription drug plan will likely be lower than the prices CymaBay might otherwise obtain. Moreover, while the MMA 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 Medicare Part D 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. 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 CymaBay's 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 CymaBay to sell its products on a profitable basis.

In March 2010 the PPACA was enacted, which includes measures to significantly change the way healthcare is financed by both governmental and private insurers. Among the provisions of the PPACA of importance to the pharmaceutical and biotechnology industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, that began in 2011;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program, created under Section 6002 of the PPACA and its implementing regulations, that manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to the U.S. Department of Health and Human Services, or HHS, information related to "payments or other transfers of value" made or distributed to physicians and teaching hospitals, and that applicable manufacturers and applicable group purchasing organizations report annually to HHS ownership and investment interests held by physicians and their immediate family members, with reporting to the Centers for Medicare & Medicaid Services, or CMS, required by March 31 of each calendar year;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;
- expansion of health care fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and
- establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending that began on January 1, 2011.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the president signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction, or joint committee, to recommend proposals in spending reductions to Congress. The joint committee did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In January 2013, the president signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our financial operations.

International Regulation

In addition to regulations in the United States, there are a variety of foreign regulations governing clinical studies and commercial sales and distribution of CymaBay's future product candidates. Whether or not FDA approval is obtained for a product, approval of a product must be obtained by the comparable regulatory authorities of foreign countries before clinical studies or marketing of the product can commence in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary greatly from country to country. In addition, certain regulatory authorities in select countries may require CymaBay to repeat previously conducted preclinical and/or clinical studies under specific criteria for approval in their respective country which may delay and/or greatly increase the cost of approval in certain markets targeted for approval by CymaBay.

Employees

As of June 30, 2014, CymaBay had 16 full-time employees, 8 of whom hold Ph.D.s and one of whom holds a Master's degree in relevant areas of expertise.

Properties

Our corporate office is located in Newark, California. We entered into a lease for our corporate office in November 2013 which commenced on January 1, 2014, and continues for a period of sixty (60) months with an option to extend the lease for an additional three years. We believe that our existing facility arrangements are adequate to meet our current requirements.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 100,000,000 shares of common stock, $0.0001 par value per share, and 10,000,000 shares of preferred stock, $0.0001 par value per share. A description of material terms and provisions of our certificate of incorporation and bylaws affecting the rights of holders of our capital stock is set forth below. The description is intended as a summary, and is qualified in its entirety by reference to our certificate of incorporation and the bylaws.

Common stock

Voting Rights. Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of the stockholders, including the election of directors. The certificate of incorporation and by-laws do not provide for cumulative voting rights in connection with election of directors unless, at the time of such election, CymaBay is subject to Section 2115(b) of the California General Corporation

Law. The affirmative vote of holders of 66 2/3% of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, will be required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, and removal of directors.

Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, the holders of outstanding shares of common stock may receive dividends, if any, as may be declared from time to time by the Board of Directors out of legally available funds. CymaBay has never issued a dividend on shares of its common stock and has no intention to do so in the future.

Liquidation. In the event of liquidation, dissolution or winding up of CymaBay, the assets legally available for distribution shall be distributed ratably to the holders of shares of common stock and preferred stock, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Rights and Preferences. Holders of common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that CymaBay may designate and issue in the future.

Fully Paid and Nonassessable. All outstanding shares of common stock are fully paid and nonassessable.

Preferred stock

Our board of directors is authorized, subject to limitations prescribed by Delaware law, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors can also increase or decrease the number of shares of any series, but not below the number of shares of that series then outstanding, without any further vote or action by the company's stockholders. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring, discouraging or preventing a change in control of CymaBay and may adversely affect the market price of CymaBay's common stock and the voting and other rights of the holders of common stock.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. We will describe in the applicable prospectus supplement the terms of the series of preferred stock being offered, including, to the extent applicable:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

- the procedures for any auction and remarketing, if applicable;
- the provisions for a sinking fund, if applicable;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

Anti-takeover effects of provisions of our certificate of incorporation and bylaws and Delaware law

Certificate of incorporation and bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws, include a number of provisions that may deter or impede hostile takeovers or changes of control or management. These provisions include:

Issuance of undesignated preferred stock. Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock enables our board of directors to make it more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.

Board of directors vacancies. Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of our entire board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.

Stockholder action; special meetings of stockholders. Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. Stockholders will not be permitted to cumulate their votes for the election of directors unless required by applicable law. Our amended and restated bylaws provide that only the chairman

of our board of directors, chief executive officer or a majority of our board of directors may call special meetings of our stockholders.

Advance notice requirements for stockholder proposals and director nominations. Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders. Our amended and restated bylaws also specify certain requirements as to the form and content of a stockholder's notice. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at annual meetings of stockholders.

CymaBay designed these provisions to enhance the likelihood of continued stability in the composition of our board of directors and its policies, to discourage certain types of transactions that may involve an actual or threatened acquisition of us, and to reduce our vulnerability to an unsolicited acquisition proposal. We also designed these provisions to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in a business combination with any interested stockholder for a period of three years following the date the person became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested holder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (a) by persons who are directors and also officers and (b) pursuant to employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 of the DGCL defines business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

Section 203 of the DGCL defines an "interested stockholder" as an entity or person who, together with the entity's or person's affiliates and associates, beneficially owns, or is an affiliate of the corporation and within

three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation. A Delaware corporation may "opt out" of these provisions with an express provision in its certificate of incorporation. We have not opted out of these provisions, which may as a result, discourage or prevent mergers or other takeover or change of control attempts of us.

Transfer Agent and Registrar

Our transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent for any series of preferred stock that we may offer under this prospectus will be named and described in the prospectus supplement related to that series.

Listing on the NASDAQ Capital Market

Our common stock is listed on the NASDAQ Capital Market the symbol "CBAY". The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on the NASDAQ Capital Market or any securities market or other exchange of the preferred stock covered by such prospectus supplement.

Warrants

As of June 30, 2014 we had warrants exercisable for 1,311,958 shares of our common stock (the "Financing Warrants"). The Financing Warrants are exercisable for a period of five (5) years from September 30, 2013, at an exercise price of $5.75 per share. The exercise prices for such Financing Warrants may be adjusted in the event of any recapitalization, reclassification, exchange, or subdivision of our outstanding shares of Common Stock. In the event we declare and pay a dividend or other distribution on the shares of our common stock, then the holder of the Financing Warrants shall be entitled to receive such dividends or distributions to the same extent as if the holder had exercised the Financing Warrant and held common stock. In the event of an acquisition or change (a "Major Transaction") of control of CymaBay, the proceeds payable to the holder of a Financing Warrant shall be determined as more completely described in Note 10 to our financial statements incorporated by reference in this prospectus. Furthermore, we may be subject to liquidated damages in the event of certain "Events of Failure" including failure to deliver shares upon exercise of the Financing Warrants, failure to remove a restrictive legend from a Financing Warrant or the underlying shares, or failure to affect a transfer of a Financing Warrant. We may be subject to liquidated damages in connection with any Event of Failure in the form of cash payments or issuance of shares of common stock in connection with any such Event of Failure, each as determined by the Black-Scholes Option Pricing Model. We may be subject to additional liquidated damages in the event of certain "Events of Default" including Events of Failure that are not cured within the requisite periods or in the event we fail to provide for appropriate payments to the holders of Financing Warrants in connection with a Major Transaction. We may be subject to liquidated damages or early mandatory termination of the Financing Warrant in connection with any Event of Default in the form of cash payments or issuance of shares of common stock in full satisfaction of the Financing Warrants, each as determined by the Black-Scholes Option Pricing Model. CymaBay further issued warrants exercisable for 414,790 shares of its common stock to NSC in its capacity as placement agent in the 2013 financing under the same terms and conditions as the Financing Warrants.

On September 30, 2013, we issued warrants to purchase an aggregate of 121,739 shares of common stock to SVB and Oxford, as partial consideration for SVB and Oxford entering into a $10,000,000 credit facility with CymaBay (the "Bank Warrants"). The Bank Warrants are exercisable for a period of ten (10) years from September 30, 2013, at an exercise price of $5.00 per share. The exercise prices for such Bank Warrants may be adjusted in the event of any recapitalization, reclassification, exchange, or subdivision of our outstanding shares of common stock. In the event CymaBay was to declare and pay a dividend or other distribution on the shares of its common stock, then upon exercise of the Bank Warrants, the holder shall be entitled to receive, without additional cost to the holder, the total number and kind of securities and property which the holder would have received had holder owned the shares of record as of the date the dividend or distribution occurred. In the event

of any merger or acquisition of CymaBay, the holder of any Bank Warrant is obligated to exercise the Bank Warrant prior to the consummation of such merger or acquisition and the Bank Warrant shall expire immediately prior to the consummation of such merger or acquisition, unless the consideration to be paid to the holders of our common stock is something other than cash or marketable securities, in which case any successor entity to CymaBay shall be obligated to assume the Bank Warrants.

Registration Rights

As of September 30, 2014, holders of a substantial number of shares of CymaBay's common stock, and holders of warrants to purchase a substantial number shares of CymaBay's common stock, have the right to require CymaBay to register with the SEC the shares of common stock and the shares of common stock issuable upon exercise of such warrants held by those holders so that those shares of common stock may be publicly resold, or, in the event any such registration statement is effective, to include those shares in any registration statement CymaBay files.

Resale Registration Statement. Pursuant to CymaBay's Registration Rights Agreement, dated September 30, 2013, as amended, entered into in connection with the 2013 financing (the "Registration Agreement"), CymaBay was obligated to file a resale registration statement (the "Resale Registration Statement") with the SEC to register the Shares, Warrant Shares and Conversion Shares (each as defined in the Registration Agreement). CymaBay filed and caused to become effective its Resale Registration Statement on December 24, 2013. In the event CymaBay fails to keep such Resale Registration Statement effective during the period required for such registration statement, then CymaBay shall pay to each holder of such affected registrable securities liquidated damages in an amount in cash equal to 1.5% of the aggregate purchase price paid by such holder for such registrable securities required to be included in such registration statement per month, provided that the amount of such liquidated damages paid to each holder may not exceed more than 25% of the aggregate purchase price paid by such holder for such registrable securities.

"Piggyback" Registration Rights. If CymaBay registers any securities for public sale (other than any registration statement relating to any employee benefit plan, any corporate reorganization or stock issued upon conversion of debt securities), holders of registrable securities under the Registration Agreement shall have the right to include their shares in the registration statement in the event the Resale Registration Statement is not effective at the time of such public sale by CymaBay. The underwriters of any underwritten offering will have the right to limit the number of shares having registration rights to be included in the registration statement.

Expenses of Registration. CymaBay will pay all expenses relating to all registrations and piggyback registrations provided for under the terms of the Registration Agreement.

Termination of Registration Rights. All registration rights described above shall terminate and be of no further force and effect at such time that all holders can sell their registrable securities under Rule 144 (1) without limitations as to volume of sales, method of sale requirements or notice requirements and (2) without the requirement for us to be in compliance with the current public information requirement under Rule 144(c)(1).

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as "discount securities," which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with "original issue discount," or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities;
- the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities, and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the Events of Default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and

- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request,
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under “Description of Debt Securities—Consolidation, Merger or Sale;”
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;

- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under "Description of Debt Securities—General" to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depositary named by us and identified in a prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and in any related free writing prospectuses that we may authorize to be distributed to you, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may may consist of warrants to purchse common stock, preferred stock or debt securities and be issued in one or more series. Warrants may be offered independently or in combination with common stock, preferred stock or debt securities offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that describe the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including:

- the offering price and aggregate number of warrants offered;

- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special U.S. federal income tax considerations of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

Governing Law

Unless we otherwise specify in the applicable prospectus supplement, the warrants and any warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depositary or warrant agent maintain for this purpose as the "holders" of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as "indirect holders" of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in "street name." Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below

under the section entitled "Special Situations When a Global Security Will Be Terminated" in this prospectus. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to

hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, if any;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices

determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters or agents that are qualified market makers on the NASDAQ Capital Market engage in passive market making transactions in the common stock on the NASDAQ Capital Market accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker’s bid, however, the passive market maker’s bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Cooley LLP, Palo Alto, California. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of CymaBay Therapeutics, Inc. at December 31, 2013 and 2012, and for each of the years then ended, appearing in this prospectus and registration statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-35318):

- our Annual Report on Form 10-K for the year ended December 31, 2013, which was filed on March 31, 2014;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, which was filed on May 15, 2014;
- our Quarterly Report on Form 10-Q for the quarter ended June 30, 2014, which was filed on August 14, 2013;
- our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014, which was filed on November 14, 2014;

- our Current Reports on Form 8-K which were filed on January 8, 2014, February 21, 2014, June 6, 2014, and November 12, 2014;
- the information specifically incorporated by reference in our Annual Report on Form 10-K for the year ended December 31, 2013, from our definitive proxy statement relating to our 2014 annual meeting of stockholders, which was filed on April 21, 2014; and
- the description of our common stock in our registration statement on Form 8-A filed with the SEC on June 16, 2014.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

CymaBay Therapeutics, Inc.
7999 Gateway Blvd., Suite 130
Newark, CA 94560
(510) 293-8800
Attn: Secretary

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Shares

Common Stock

PROSPECTUS SUPPLEMENT

JonesTrading

LifeSci Capital LLC

, 2017