

Theravance Biopharma, Inc.
Form 424B5
April 29, 2016

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Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-205275

PROSPECTUS SUPPLEMENT
(To Prospectus dated July 16, 2015)

4,765,000 Shares

Theravance Biopharma, Inc.

Ordinary Shares

We are offering 4,765,000 of our ordinary shares. Our ordinary shares are listed on The NASDAQ Global Market under the symbol "TBPH." The last reported sale price of our ordinary shares on April 28, 2016 was \$21.16 per share.

The underwriters have a 30-day option to purchase up to 714,750 additional shares from us.

Investing in our Ordinary Shares involves risks. See "Risk Factors" beginning on page S-9.

| | Price to Public | Underwriting Discounts and Commissions(1) | Proceeds to Theravance Biopharma, Inc. |
|-----------|------------------------|--|---|
| Per Share | \$21.00 | \$1.26 | \$19.74 |
| Total | \$100,065,000.00 | \$6,003,900.00 | \$94,061,100.00 |

(1) We refer you to "Underwriters" beginning on page S-55 of this prospectus supplement for further information regarding underwriter compensation.

The underwriters expect to deliver the ordinary shares against payment on or about May 4, 2016.

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 prospectus to which it relates is truthful or complete. Any representation to the contrary is a criminal offense.

Leerink Partners

Evercore ISI

Guggenheim Securities

Baird

The date of this prospectus supplement is April 28, 2016.

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ABOUT THIS PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING PROSPECTUS

This document is in two parts. The first part is the prospectus supplement, which describes the specific terms of this offering 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, gives more general information about securities we may offer from time to time, some of which does not apply to this offering. To the extent the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus, the information in this prospectus supplement controls.

We have not, and the underwriters have not, authorized anyone to provide you with different information than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus to which we have referred you. 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 not assume that the information in this prospectus supplement, the accompanying prospectus or any free writing prospectus we may authorize to be delivered to you, including any information incorporated by reference, is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates. You should also read and consider the information in the documents we have referred you to in the sections of the prospectus supplement entitled "Where You Can Find More Information" and "Incorporation by Reference."

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. Some of the documents referred to herein have been filed as exhibits to the registration statement of which this prospectus supplement and accompanying prospectus are a part, while others are incorporated by reference from our previously filed periodic reports or the description of our ordinary shares contained in the Registration Statement No. 001-36033 on Form 10, as amended and filed with the Securities and Exchange Commission (the "SEC") on May 7, 2014, and amendments thereto, including their exhibits, and you may obtain copies of these documents as described below under "Where You Can Find More Information" and "Incorporation by Reference."

We have not taken any action to permit an offering of our ordinary shares outside the United States or to permit the possession or distribution of this prospectus supplement or the accompanying prospectus outside the United States. Persons outside the United States who come into possession of this prospectus supplement and/or the accompanying prospectus must inform themselves about and observe any restrictions relating to the offering of our ordinary shares and the distribution of this prospectus supplement and the accompanying prospectus outside of the United States.

In this prospectus supplement and the accompanying prospectus, unless otherwise indicated or the context otherwise requires, the terms "Theravance Biopharma," "company," "we," "our," and "us" refer to Theravance Biopharma, Inc. and its consolidated subsidiaries.

FORWARD-LOOKING STATEMENTS

This prospectus supplement contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Such forward-looking statements involve substantial risks, uncertainties and assumptions. All statements in this prospectus supplement, other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans, intentions, expectations,

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objectives and this offering (including the anticipated use of the net proceeds therefrom) could be forward-looking statements. The words "aim," "anticipates," "believes," "contemplates," "continue," "could," "designed," "developed," "drive," "estimates," "expects," "goal," "intends," "may," "mission," "opportunities," "plans," "potential," "predicts," "projects," "pursuing," "represents," "seeks," "should," "suggest," "target," "will," "would" and similar expressions (including the negatives thereof) are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions, expectations or objectives disclosed in our forward-looking statements and the assumptions underlying our forward-looking statements may prove incorrect. Therefore, you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and objectives disclosed in the forward-looking statements that we make.

Factors that we believe could cause actual results or events to differ materially from our forward-looking statements include, but are not limited to, those discussed below, in the prospectus supplement, the accompanying prospectus and in the documents incorporated herein and therein by reference, in the sections "Summary" and "Risk Factors" in this prospectus supplement and in the sections "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" in our Annual Report on Form 10-K for the year ended December 31, 2015 and elsewhere in this prospectus supplement, the accompanying prospectus and in the documents incorporated herein and therein by reference. Our forward-looking statements in this prospectus supplement are based on current expectations and we do not assume any obligation to update any forward-looking statements.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act relating to the ordinary shares offered by this prospectus supplement and accompanying prospectus. This prospectus supplement and the accompanying prospectus do not contain all of the information in the registration statement, parts of which we have omitted, as allowed under the rules and regulations of the SEC. You should refer to the registration statement for further information with respect to us and our ordinary shares. Statements contained in this prospectus supplement and the accompanying prospectus as to the contents of any contract or other document are not necessarily complete and, in each instance, we refer you to the copy of each contract or document filed as an exhibit to the registration statement. Copies of the registration statement, including exhibits, may be inspected without charge at the SEC's principal office in Washington, D.C., and you may obtain copies from this office upon payment of the fees prescribed by the SEC.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with them, 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 information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below (except the information contained in such documents to the extent "furnished" and not "filed") and any future filings we make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (except the information contained in such documents to the extent "furnished" and not "filed"):

our annual report on Form 10-K for the fiscal year ended December 31, 2015;

the information in our Definitive Proxy Statement on Schedule 14A, filed on March 25, 2016 to the extent incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2015;

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the description of our ordinary shares and preferred stock purchase rights contained in our Registration Statement No. 001-36033 on Form 10 as amended and filed with the SEC on May 7, 2014, including any amendment or report filed for the purpose of updating such description; and

our current reports on Form 8-K, filed on January 11, 2016 (but only with respect to Item 2.02), on February 25, 2016 (but only with respect to those portions of Item 8.01 that were "filed" for the purposes of Section 18 of the Exchange Act) and on March 14, 2016.

You may request, and we will provide you with, a copy of these filings at no cost by calling us at (650) 808-6000 or by writing to us at the following address:

Theravance Biopharma, Inc.
c/o Theravance Biopharma US, Inc.
901 Gateway Boulevard
South San Francisco, CA 94080
Attn: Investor Relations

Any statement contained in a document incorporated or deemed to be incorporated by reference into this prospectus supplement or the accompanying prospectus shall be deemed to be modified or superseded for the purposes of this prospectus supplement or the accompanying prospectus to the extent that a statement contained in this prospectus supplement (or in any document incorporated by reference therein) or the accompanying prospectus or in any other subsequently filed document that is or is deemed to be incorporated by reference into this prospectus supplement modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement or the accompanying prospectus.

To the extent that any information contained in any Current Report on Form 8-K, or any exhibit thereto, was furnished to, rather than filed with, the SEC, such information or exhibit is specifically not incorporated by reference in this prospectus supplement or the accompanying prospectus.

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SUMMARY

You should read the following summary together with the entire prospectus supplement and accompanying prospectus and the documents incorporated by reference herein and therein, including our consolidated financial statements and related notes. You should carefully consider, among other things, the matters discussed in the section entitled "Risk Factors" in this prospectus supplement.

Theravance Biopharma, Inc.

Overview

We are a diversified biopharmaceutical company with the core purpose of creating medicines that make a difference in the lives of patients suffering from serious illness.

Our pipeline of internally discovered product candidates includes potential best-in-class medicines to address the unmet needs of patients being treated for serious conditions primarily in the acute care setting. VIBATIV® (telavancin), our first commercial product, is a once-daily dual-mechanism antibiotic approved in the U.S., Europe and certain other countries for certain difficult-to-treat infections. Revedfenacin (TD-4208) is a long-acting muscarinic antagonist ("LAMA") being developed as a potential once-daily, nebulized treatment for chronic obstructive pulmonary disease ("COPD"). Our neprilysin ("NEP") inhibitor program is designed to develop selective NEP inhibitors for the treatment of a range of major cardiovascular and renal diseases, including acute and chronic heart failure, hypertension and chronic kidney diseases such as diabetic nephropathy. Our research efforts are focused in the areas of inflammation and immunology, with the goal of designing medicines that provide targeted drug delivery to tissues in the lung and gastrointestinal tract in order to maximize patient benefit and minimize risk. The first program to emerge from this research is designed to develop GI-targeted pan-Janus kinases ("JAK") inhibitors for the treatment of a range of inflammatory intestinal diseases.

In addition, we have an economic interest in future payments that may be made by Glaxo Group Limited or one of its affiliates ("GSK") pursuant to its agreements with Innoviva, Inc. ("Innoviva") (known as Theravance, Inc. prior to January 7, 2016) relating to certain drug development programs, including the combination of fluticasone furoate, umeclidinium, and vilanterol (the "Closed Triple").

On June 1, 2014, Innoviva separated its late-stage respiratory assets partnered with GSK from its biopharmaceutical operations by transferring its discovery, development and commercialization operations (the "Biopharmaceutical Business") and contributing \$393.0 million of cash, cash equivalents and marketable securities into its then wholly-owned subsidiary Theravance Biopharma. On June 2, 2014, Innoviva made a pro rata dividend distribution to its stockholders of record on May 15, 2014 of one ordinary share of Theravance Biopharma for every three and one half shares of Innoviva common stock outstanding on the record date (the "Spin-Off"). The Spin-Off resulted in Theravance Biopharma operating as an independent, publicly-traded company. Prior to June 2, 2014, Innoviva operated the Biopharmaceutical Business.

Our Programs

The table below summarizes the status of our approved product and our most advanced product candidates for internal development or co-development. Our research and development activities are concentrated primarily on four therapeutic areas infectious disease, respiratory, gastrointestinal disease and cardiovascular and renal disease and our commercial infrastructure is focused primarily on the acute care setting. The table also includes the status of the respiratory programs in which we have an economic interest and are being developed by GSK pursuant to agreements between Innoviva and GSK ("GSK-Partnered Respiratory Programs"). These programs consist of the Closed Triple program, the Inhaled Bifunctional Muscarinic Antagonist-Beta2 Agonist ("MABA") program and other

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future products that may be combined with the Closed Triple or MABA. We have an economic interest in these programs through our interest in Theravance Respiratory Company, LLC ("TRC"), a limited liability company managed by Innoviva. The status of these programs consists solely of publicly available information.

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R-Pharm is conducting a Phase 3 clinical study of TD-1792 in complicated skin and skin structure infections ("cSSSI"), caused by gram-positive bacteria with clinical sites in the Russian Federation and the country of Georgia.

**

The information regarding the Closed Triple and the MABA programs is based solely upon publicly available information and may not reflect the most recent developments under the programs.

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Glossary of Defined Terms used in Table Above:

COPD: Chronic Obstructive Pulmonary Disease;

cSSSI: Complicated Skin and Skin Structure Infections;

FDC: Fixed-dose Combination;

FF: Fluticasone Furoate;

GI: Gastrointestinal;

HABP/VABP: Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia;

HCV: Hepatitis C Virus;

ICS: Inhaled Corticosteroid;

MABA: Bifunctional Muscarinic Antagonist-Beta₂ Agonist;

MRSA: Methicillin-Resistant Staphylococcus Aureus;

nOH: Neurogenic Orthostatic Hypotension;

OIC: Opioid Induced Constipation;

UMEC: Umeclidinium;

VI: Vilanterol;

"**Status**" in the table above refers to the most advanced stage of clinical development that has been completed or is in process;

Phase 1: initial clinical safety testing into patients or healthy human volunteers, or studies directed toward understanding the mechanisms of action of the drug;

Phase 2: further clinical safety testing and preliminary efficacy testing in a limited patient population;

Phase 3: evaluation of clinical efficacy and safety within an expanded patient population;

Filed: a marketing application has been submitted to a regulatory authority; and

Approved: approved for marketing.

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The table below summarizes the target completion period for the key milestones associated with our priority programs. The information with respect to our financial assets is comprised solely of information reported by GSK.

Priority Programs:

| Program | Milestone | Target |
|-------------------------|--|------------------------|
| VIBATIV® (telavancin) | Concurrent Bacteremia & HABP/VABP or cSSSI PDUFA | Q2 2016 |
| Telavancin | Complete Phase 3 Bacteremia Study | 2017/2018 |
| Revefenacin (TD-4208) | Complete Phase 3 Efficacy Studies | Late Q3/ early Q4 2016 |
| Revefenacin (TD-4208) | Complete Phase 3 LTSS | 2017 |
| Revefenacin (TD-4208) | US Regulatory Filing | Late 2017 |
| TD-1473 (JAK inhibitor) | Complete Phase 1 | Q2 2016 |
| TD-0714 (NEP inhibitor) | Complete Phase 1 (incl. target engagement) | 2H 2016 |

Financial Assets*:

| Program | Milestone | Target |
|----------------------------|-------------------------------|--------|
| Closed Triple (FF/UMEC/VI) | Complete Phase 3 FULFIL Study | 2016 |
| Closed Triple (FF/UMEC/VI) | EU Regulatory Filing | 2016 |
| Closed Triple (FF/UMEC/VI) | Complete Phase 3 IMPACT Study | 2017 |
| Closed Triple (FF/UMEC/VI) | US Regulatory Filing | 2018 |

*

Regulatory and clinical milestones as reported by GSK.

Recent Developments

We are currently finalizing our financial results for the three months ended March 31, 2016. The financial results discussed below for the three months ended March 31, 2016 are preliminary and subject to completion of financial and operating closing procedures. The results below are not a comprehensive statement of our financial results or operating metrics for this period and our actual results and metrics may differ materially from these amounts following the completion of our financial and operating closing procedures, or as a result of other adjustments or developments that may arise before the results for this period are finalized. In addition, even if our actual results and metrics are consistent with these preliminary results, those results or developments may not be indicative of results or developments in subsequent periods.

We expect to report that our revenue from net U.S. product sales was between \$3.2 million and \$3.4 million for the three months ended March 31, 2016 compared to \$1.3 million for the same period in 2015 and \$3.1 million for the three months ended December 31, 2015.

We also expect to report that our cash, cash equivalents and marketable securities were approximately \$214 million and our receivables from collaborative arrangements were approximately \$37 million as of March 31, 2016. As of December 31, 2015, our cash, cash equivalents and marketable securities totaled \$215.3 million and our receivables from collaborative arrangements were \$35.2 million.

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Corporate Information

Theravance Biopharma was incorporated in the Cayman Islands in July 2013 under the name Theravance Biopharma, Inc. While the Company is incorporated under Cayman Island law, the Company became an Irish tax resident effective July 1, 2015. Our corporate address in the Cayman Islands is P.O. Box 309, Uglan House, Grand Cayman, KY1-1104, Cayman Islands and the principal office of our wholly-owned U.S. operating subsidiary Theravance Biopharma US, Inc. is 901 Gateway Boulevard, South San Francisco, California 94080.

Our internet address is www.theravance.com. Information contained on or accessible through our website does not constitute a part of this prospectus supplement or the accompanying prospectus.

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THE OFFERING

| | |
|---|---|
| Ordinary shares offered by us | 4,765,000 shares |
| Option to purchase additional shares | 714,750 shares |
| Ordinary shares to be outstanding immediately after this offering | 46,217,277 shares (46,932,027 shares if the underwriters exercise their option to purchase additional shares in full) |
| Use of proceeds | We intend to use the net proceeds from this offering for general corporate purposes, which may include, among other things, research activities, preclinical and clinical development of product candidates, manufacture of pre-clinical, clinical and commercial drug supplies, selling and marketing expenses, capital expenditures, working capital, general and administrative expenses and acquisitions of technology or drug candidates. We do not currently have any commitments with regard to any such acquisitions or other strategic transactions. |
| Risk factors | See "Risk Factors" beginning on page S-9 for a discussion of factors you should consider carefully before making an investment decision. |
| The NASDAQ Global Market Symbol | TBPH |
| The number of ordinary shares that will be outstanding after this offering is based on 41,452,277 ordinary shares outstanding as of March 31, 2016, and excludes: | |

2,259,986 ordinary shares issuable upon the exercise of outstanding options to purchase our ordinary shares as of March 31, 2016 having a weighted-average exercise price of \$22.83 per share;

854,958 ordinary shares reserved for issuance pursuant to future awards under our 2013 Equity Incentive Award Plan, and any addendums thereto;

171,706 ordinary shares reserved for issuance pursuant to future awards under our 2014 New Employee Equity Incentive Plan;

1,308,954 ordinary shares reserved for issuance pursuant to future awards under our 2013 Employee Share Purchase Plan; and

4,404,992 ordinary shares issuable upon vesting of outstanding restricted share units.

In addition, excluded from the number of ordinary shares shown above are 489,664 ordinary shares issued in April 2016 under at-the-market offerings pursuant to our sales agreement with Cantor Fitzgerald & Co.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares.

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The following tables present our summary consolidated statements of operations data for the years ended December 31, 2015, 2014 and 2013 and our consolidated balance sheet data as of December 31, 2015 and 2014, which are derived from our audited financial statements that are incorporated by reference in this prospectus supplement, and are qualified by reference to such financial statements. You should read this information in conjunction with our audited consolidated financial statements, including the related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the year ended December 31, 2015. Our historical results are not necessarily indicative of the results that may be expected in the future.

| | Year Ended December 31, | | |
|--|--|--------------|--------------|
| | 2015 | 2014 | 2013 |
| | (In thousands, except per share data) | | |
| Consolidated Statements of Operations Data | | | |
| Product sales | \$ 9,408 | \$ 4,418 | \$ |
| Revenue from collaborative arrangements | 32,718 | 7,270 | 226 |
| Total revenue | 42,126 | 11,688 | 226 |
| Costs and expenses: | | | |
| Cost of goods sold(1) | 4,657 | 4,058 | |
| Research and development | 129,165 | 168,522 | 120,579 |
| Selling, general and administrative | 90,203 | 71,647 | 35,931 |
| Total costs and expenses(2) | 224,025 | 244,227 | 156,510 |
| Loss from operations | (181,899) | (232,539) | (156,284) |
| Interest and other income | 631 | 1,865 | |
| Loss before income taxes | (181,268) | (230,674) | (156,284) |
| Provision for income taxes | 951 | 6,364 | |
| Net loss | \$ (182,219) | \$ (237,038) | \$ (156,284) |
| Basic and diluted net loss per share | \$ (5.34) | \$ (7.46) | \$ (4.92) |
| Shares used to compute basic and diluted net loss per share(3) | 34,150 | 31,755 | 31,741 |

| | As of December 31, | |
|--|---------------------------|-------------|
| | 2015 | 2014 |
| | (In thousands) | |
| Consolidated Balance Sheets Data | | |
| Cash, cash equivalents and marketable securities | \$ 215,294 | \$ 306,010 |
| Working capital | 188,002 | 234,114 |
| Total assets | 300,116 | 337,771 |
| Long-term liabilities(4) | 7,581 | 6,728 |

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| | | |
|----------------------------|-----------|-----------|
| Accumulated deficit | (321,556) | (139,337) |
| Total shareholders' equity | 243,065 | 289,787 |

(1)

For the years ended December 31, 2015 and 2014, cost of goods sold includes charges of \$1.9 million and \$2.9 million, respectively, for the write-down of VIBATIV inventory due to the dating of the product.

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- (2) The following table discloses the allocation of share-based compensation expense included in total operating expenses:

| | Year Ended December 31, | | |
|---------------------------------------|-------------------------|------------------|------------------|
| | 2015 | 2014 | 2013 |
| | (In thousands) | | |
| Research and development | \$ 25,770 | \$ 21,191 | \$ 15,444 |
| Selling, general and administrative | 28,280 | 22,043 | 7,032 |
| Total share-based compensation | \$ 54,050 | \$ 43,234 | \$ 22,476 |

- (3) Prior to our Spin-Off in June 2014, we operated as part of Innoviva and not as a separate entity. As a result, the calculation of basic and diluted net loss per share assumes that the 32,260,105 ordinary shares issued to Innoviva stockholders in connection with the Spin-Off, less the number of ordinary shares subject to forfeiture, were outstanding from the beginning of 2013 and 2014.
- (4) Long-term liabilities include the long-term portion of deferred revenue of \$952,000 and \$712,000 as of December 31, 2015 and December 31, 2014, respectively.

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RISK FACTORS

Investing in our ordinary shares involves risk. Prior to making a decision about investing in our ordinary shares, you should carefully consider the specific factors discussed in this section and under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in our Annual Report on Form 10-K for the year ended December 31, 2015, which is incorporated by reference in this prospectus supplement, together with all of the other information contained in this prospectus supplement and the accompanying prospectus, or incorporated by reference herein or therein. The risks described in this prospectus supplement and the accompanying prospectus, or incorporated by reference herein or therein are not the only risks facing the Company. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition and/or operating results.

RISKS RELATING TO THE COMPANY

We anticipate that we will incur losses for the foreseeable future. We may never achieve or sustain profitability.

First as part of Innoviva, Inc. (known as Theravance, Inc. prior to January 7, 2016), and since June 2, 2014 as Theravance Biopharma, we have been engaged in discovery and development of compounds and product candidates since mid-1997. We may never generate sufficient revenue from the sale of medicines, royalties on sales by our partners or from our interest in TRC to achieve profitability. During the years ended December 31, 2015, 2014 and 2013, we recognized losses of \$182.2 million, \$237.0 million and \$156.3 million, respectively, which are reflected in the Shareholders' Equity on our consolidated balance sheets. We reflect cumulative net loss incurred and retained after June 2, 2014, the effective date of the Spin-Off, as accumulated deficit on our consolidated balance sheets. We expect to continue to incur net losses at least over the next several years as we continue our drug discovery and development efforts and incur significant preclinical and clinical development costs related to our current product candidates and commercialization and development costs relating to VIBATIV® (telavancin). In particular, to the extent we advance our product candidates into and through later stage clinical studies without a partner, we will incur substantial expenses. We are also making additional investments in telavancin, our antibiotic that has been approved for certain difficult-to-treat infections. For example, in February 2015 we initiated a Phase 3 registrational study of telavancin for bacteremia and a patient registry study. We are incurring all of the costs and expenses associated with the commercialization of VIBATIV in the U.S., including the creation of an independent sales and marketing organization with appropriate technical expertise, supporting infrastructure and distribution capabilities, expanded medical affairs presence, manufacturing and third party vendor logistics and consultant support, and post-marketing studies. Our commitment of resources to VIBATIV, to the continued development of our existing product candidates and to our discovery programs will require significant additional funding. Our operating expenses also will increase if, among other things:

our earlier stage potential products move into later stage clinical development, which is generally more expensive than early stage development;

additional preclinical product candidates are selected for clinical development;

we pursue clinical development of our potential or current products in new indications;

we increase the number of patents we are prosecuting or otherwise expend additional resources on patent prosecution or defense; or

we acquire or in-license additional technologies, product candidates, products or businesses.

Other than revenues from sales of VIBATIV, our only approved medicine, and potential payments under collaboration agreements, we do not expect to generate sales revenues from our programs for

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the foreseeable future. Since we or our collaborators or licensees may not successfully develop additional products, obtain required regulatory approvals, manufacture products at an acceptable cost or with appropriate quality, or successfully market and sell such products with desired margins, our expenses may continue to exceed any revenues we may receive.

In the absence of substantial licensing payments, contingent payments or other revenues from third-party collaborators, royalties on sales of products licensed under our intellectual property rights, future revenues from VIBATIV and product candidates in development that receive regulatory approval or other sources of revenues, we will continue to incur operating losses and will require additional capital to execute our business strategy. The likelihood of reaching, and time required to reach, and then to sustain, profitability are highly uncertain. As a result, we expect to continue to incur substantial losses for the foreseeable future. We are uncertain when or if we will ever be able to achieve or sustain profitability. Failure to become and remain profitable would adversely affect the price of our securities and our ability to raise capital and continue operations.

If additional capital is not available, we may have to curtail or cease operations or we could be forced to share our rights to commercialize our product candidates with third parties on terms that may not be favorable to us.

Based on our current operating plans and financial forecasts, we believe that our cash, cash equivalents and marketable securities will be sufficient to meet our anticipated operating needs for at least the next twelve months. If our current operating plans or financial forecasts change, we may require or seek additional funding sooner in the form of public or private equity or equity-linked offerings, debt financings or additional collaborations and licensing arrangements. For example, if we choose to progress any of our product candidates into later-stage development on our own, our capital needs would increase substantially. We also are making significant investments in telavancin, our approved antibiotic, which increases our operating expenses. For example, in February 2015 we announced initiation of a Phase 3 registrational study for bacteremia and initiation of a patient registry study. In addition, in 2015 we substantially increased the number of sales representatives and medical science liaisons supporting physician education on the proper usage of VIBATIV in the U.S. and at the end of 2015, we had approximately 50 sales representatives in the field.

We may need to raise additional capital in the future to, among other things:

- fund our discovery efforts and research and development programs;
- fund our commercialization strategies for VIBATIV;
- progress mid-to-late stage product candidates into later stage development, if warranted;
- respond to competitive pressures; and
- acquire complementary businesses or technologies.

Our future capital needs depend on many factors, including:

- the scope, duration and expenditures associated with our discovery efforts and research and development programs;
- continued scientific progress in these programs;
- the extent to which we encounter technical obstacles in our research and development programs;
- the outcome of potential licensing or partnering transactions, if any;

competing technological developments;

the extent of our proprietary patent position in televancin and our product candidates;

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our facilities expenses, which will vary depending on the time and terms of any facility lease or sublease we may enter into, and other operating expenses;

the scope and extent of the expansion of our sales and marketing efforts;

potential litigation and other contingencies; and

the regulatory approval process for our product candidates.

We may not be able to obtain additional financing on terms favorable to us, if at all. General market conditions may make it very difficult for us to seek financing from the capital markets. We may be required to relinquish rights to our technologies, product candidates or territories, or grant licenses on terms that are not favorable to us, in order to raise additional funds through collaborations or licensing arrangements. We may sequence pre-clinical and clinical studies as opposed to conducting them concomitantly in order to conserve resources, or delay, reduce or eliminate one or more of our research or development programs and reduce overall overhead expenses. If we are unable to raise additional capital or obtain future funding in sufficient amounts or on terms acceptable to us, we may have to make reductions in our workforce and may be prevented from continuing our discovery, development and commercialization efforts and exploiting other corporate opportunities. This would likely harm our business, prospects and financial condition and cause the price of our securities to fall.

We may seek to obtain future financing through the issuance of debt or equity, which may have an adverse effect on our shareholders or may otherwise adversely affect our business.

If we raise funds through the issuance of debt, convertible debt or equity, any debt securities or preferred shares issued will have rights, preferences and privileges senior to those of holders of our ordinary shares in the event of liquidation. In such event, there is a possibility that once all senior claims are settled, there may be no assets remaining to pay out to the holders of ordinary shares. In addition, if we raise funds through the issuance of additional equity, whether through private placements or public offerings, such an issuance would dilute ownership of our current shareholders that do not participate in the issuance. For example, in connection with entering into a collaboration agreement with Mylan, Inc. ("Mylan") for the development and commercialization of a nebulized formulation of our LAMA revefenacin (TD-4208) in February 2015, Mylan made a \$30.0 million equity investment in us by purchasing 1,585,790 newly issued ordinary shares, which issuance resulted in dilution of ownership to our shareholders. By way of further example, in October 2015, funds managed by Woodford Investment Management LLP (collectively, the "Woodford Funds") made a \$55.0 million equity investment in us by purchasing 3,859,649 newly issued ordinary shares, and in March 2016, GSK made an approximately \$23.0 million equity investment in us by purchasing 1,301,015 newly issued ordinary shares, which issuances resulted in dilution of ownership to our shareholders. In addition, if we seek to raise funds and this becomes known publicly, the market price of our shares could decline upon the expectation of dilution, regardless of whether dilution actually occurs. In July 2015, our shelf registration statement on Form S-3 for the potential offering, issuance and sale by us of up to a maximum aggregate offering price of \$250.0 million of our debt securities, ordinary shares, and/or warrants was declared effective. Up to \$50.0 million of the maximum aggregate offering price of \$250.0 million under the registration statement may be issued and sold pursuant to an at-the-market offering program for sales of our ordinary shares under a sales agreement with Cantor Fitzgerald & Co. ("Cantor"). In October 2015, we used \$55.0 million of the available financing capacity under the registration statement in the foregoing sale of ordinary shares to the Woodford Funds and in March and April of 2016, we used approximately \$15 million of the available financing capacity under the registration statement pursuant to our at-the-market offering program for sales of approximately 770,000 ordinary shares under the foregoing sales agreement with Cantor. If we are unable to obtain any needed additional funding, we may be required to reduce the scope of, delay, or eliminate some or all of, our planned research, development and commercialization activities or to license to third parties

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the rights to develop and/or commercialize products or technologies that we would otherwise seek to develop and/or commercialize ourselves or on terms that are less attractive than they might otherwise be, any of which could materially harm our business.

Furthermore, the terms of debt securities may impose restrictions on our operations, which may include limiting our ability to incur additional indebtedness, pay dividends on or repurchase our share capital, or make certain acquisitions or investments. In addition, we may be subject to covenants requiring us to satisfy certain financial tests and ratios, and our ability to satisfy such covenants may be affected by events outside of our control.

If we are unable to enter into future collaboration arrangements or if any such collaborations with third parties are unsuccessful, we will be unable to fully develop and commercialize all of our product candidates and our business will be adversely affected.

We have collaborations with a number of third parties including Mylan for the development and commercialization of a nebulized formulation of revefenacin (TD-4208), our LAMA compound, Alfa Wassermann S.p.A. ("Alfa Wassermann") for velusetrag, Clinigen Group plc ("Clinigen") for VIBATIV for the European Union, and with other companies for regional development and commercialization of VIBATIV. Also, through our interest in TRC we may participate economically in Innoviva's collaborations with GSK with respect to the GSK-Partnered Respiratory Programs and we received non-marketable equity securities in connection with our September 2015 licensing agreement with Trek Therapeutics, PBC. Additional collaborations will likely be needed to fund later stage development of certain programs that have not been licensed to a collaborator, such as our NEP inhibitor program and axelopran (TD-1211) for opioid-induced constipation and to commercialize the product candidates in these programs if approved by the necessary regulatory authorities. We may also seek collaboration arrangements with additional third parties to pursue the future commercialization of VIBATIV in regions where it is not currently partnered. Collaborations with third parties regarding these programs or our other programs may require us to relinquish material rights, including revenue from commercialization of our medicines, or to assume material ongoing development obligations that we would have to fund. These collaboration arrangements are complex and time-consuming to negotiate, and if we are unable to reach agreements with third-party collaborators, we may fail to meet our business objectives and our financial condition may be adversely affected. We face significant competition in seeking third-party collaborators. We may be unable to find third parties to pursue product collaborations on a timely basis or on acceptable terms. Furthermore, for any collaboration, we may not be able to control the amount of time and resources that our partners devote to our product candidates and our partners may choose to prioritize alternative programs. Our inability to successfully collaborate with third parties would increase our development costs and may cause us to choose not to continue development of certain product candidates, would limit the likelihood of successful commercialization of some of our product candidates and could cause the price of our securities to fall.

We do not control TRC and, in particular, have no control over or access to non-public information about the respiratory programs that Innoviva partnered with GSK and assigned to TRC in connection with the Spin-Off.

Innoviva has assigned to TRC its strategic alliance agreement with GSK and all of its rights and obligations under its LABA collaboration agreement other than with respect to RELVAR® ELLIPTA®/BREO® ELLIPTA®, ANORO® ELLIPTA® and vilanterol monotherapy. Our equity interest in TRC entitles us to an 85% economic interest in any future payments made by GSK under the strategic alliance agreement and under the portion of the collaboration agreement assigned to TRC (the "GSK Agreements"). Our equity interest covers various drug programs including the Closed Triple combination of fluticasone furoate (FF)/umeclidinium (UMEC)/vilanterol (VI) (ICS/LAMA/LABA) and the MABA program, as monotherapy and in combination with other therapeutically active components, such as an inhaled corticosteroid ("ICS"), and any other product or combination of

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products that may be discovered and developed in the future under the GSK Agreements. Our economic interest does not include any payments by GSK associated with RELVAR® ELLIPTA®/BREO® ELLIPTA®, ANORO® ELLIPTA® or vilanterol monotherapy. Innoviva controls TRC and, except for certain limited consent rights, we have no right to participate in the business and affairs of TRC. Innoviva has the exclusive right to appoint TRC's manager who, among other things, is responsible for the day-to-day management of the GSK-Partnered Respiratory Programs and exercises the rights relating to the GSK-Partnered Respiratory Programs. As a result, we have no rights to participate in or access to non-public information about the development and commercialization of the GSK-Partnered Respiratory Programs and no right to enforce rights under the GSK Agreements assigned to TRC. Moreover, we have many of the same risks with respect to our and TRC's dependence on GSK as we have with respect to our dependence on our own partners.

If the GSK-Partnered Respiratory Programs in which we have a substantial economic interest, including the Closed Triple program and MABA program, encounter delays, do not demonstrate safety and efficacy, are terminated, or if there are any adverse developments or perceived adverse developments with respect to these programs, our business will be harmed, and the price of our securities could fall.

We have no access to confidential information regarding the progress of, or plans for, the GSK-Partnered Respiratory Programs, including the Closed Triple program and the MABA program, and we have little, if any, ability to influence the progress of those programs because our interest in these programs is only through our economic interest in TRC, which is controlled by Innoviva. However, if any of the GSK-Partnered Respiratory Programs assigned to TRC in which we have a substantial economic interest, including the Closed Triple program and MABA program, encounter delays, do not demonstrate safety and efficacy, are terminated, or if there are any adverse developments or perceived adverse developments with respect to such programs, our business will be harmed, and the price of our securities could fall. Examples of such adverse developments include, but are not limited to:

GSK deciding to delay or halt development of any of the GSK-Partnered Respiratory Programs assigned to TRC in which we have a substantial economic interest, including the Closed Triple, GSK961081 ('081), the lead compound in the MABA program, or '081/FF;

the U.S. Food and Drug Administration ("FDA") and/or other regulatory authorities determining that any of the studies under these programs do not demonstrate adequate safety or efficacy, or that additional non-clinical or clinical studies are required with respect to such programs;

safety, efficacy or other concerns arising from clinical or non-clinical studies in these programs; or

any particular FDA requirements or changes in FDA policy or guidance regarding these programs.

VIBATIV may not be broadly accepted by physicians, patients, third party payors, or the medical community in general, which would have a material, adverse effect on our business.

The commercial success of VIBATIV depends upon its acceptance by physicians, patients, third party payors and the medical community in general. VIBATIV may not be sufficiently accepted by these parties. VIBATIV competes with vancomycin (which accounts for a substantial majority of patient treatment days) and linezolid, both relatively inexpensive generic drugs that are manufactured by a variety of companies, and a number of existing antibacterials manufactured and marketed by major pharmaceutical companies and others, and may compete against new antibacterials that are not yet on the market. In addition, sales of a generic version of daptomycin could begin in 2016. If we are unable to demonstrate to physicians that, based on experience, clinical data, side effect profiles and other

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factors, VIBATIV is a preferred injectable treatment for treating the infections for which it is indicated, we may never generate significant revenue from VIBATIV. In that case we may in the future reassess the VIBATIV business and respond in a number of ways which could include, for example, reducing our investment in commercialization and development efforts or other actions, any of which could cause the price of our securities to fall. In addition, if we fail to meet expectations about our net sales of VIBATIV and our VIBATIV commercialization strategy, the price of our securities could fall. For example, we reduced our projected U.S. net sales target for VIBATIV for 2015 more than once.

The degree of market acceptance of VIBATIV, the rate of our VIBATIV sales and our ability to generate revenues through sales of VIBATIV depends on a number of factors, including, but not limited to:

the experiences of physicians, patients and payors with the use of VIBATIV;

the market price of VIBATIV relative to competing therapies;

the timing, frequency and impact of price changes or changes to pricing programs;

our customer mix;

any adverse developments or perceived adverse developments with respect to whether Pfizer Inc. ("Pfizer") acquisition of Hospira Worldwide, Inc. ("Hospira") may lead to changes in Hospira's operations which may adversely impact our single source of supply for VIBATIV drug product;

the advantages and disadvantages of VIBATIV compared to alternative therapies;

our ability to educate the medical community about the appropriate circumstances for use of VIBATIV;

the acceptance of VIBATIV onto formulary by hospitals and healthcare systems;

our ability to attract, train and retain appropriate numbers of sales and marketing personnel in the U.S.;

our ability to attract, train and retain medical science liaisons in the U.S. supporting physician education on the proper usage of VIBATIV;

the effectiveness of sales personnel in obtaining access to and educating adequate numbers of physicians about prescribing VIBATIV in appropriate clinical situations;

the lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

the reimbursement policies of government and third party payors, including the amount of chargebacks and government rebates.

We are developing the capability to market, sell and distribute VIBATIV in the U.S. without a partner and we may bear similar costs with respect to additional products in the future, which subjects us to certain risks.

We evaluate commercial strategy on a product by product basis either to engage pharmaceutical or other healthcare companies with an existing sales and marketing organization and distribution system to market, sell and distribute our products or to commercialize a product ourselves. However, we may not be able to establish these sales and distribution relationships on acceptable terms, or at all, or may encounter difficulties in commercializing a product ourselves. For any of our product candidates that receive regulatory approval in the future and are not covered by our current collaboration agreements, we will need a partner in order to commercialize such products unless we establish independent sales, marketing and distribution capabilities with appropriate technical expertise and supporting infrastructure.

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VIBATIV was returned by Astellas Pharma Inc. ("Astellas"), our former VIBATIV collaboration partner, in January 2012, and Astellas is entitled to a ten-year, 1% royalty on future net sales of VIBATIV. On August 14, 2013, we (at the time with Innoviva) announced the reintroduction of VIBATIV to the U.S. market with the commencement of shipments into the wholesaler channel and as of the end of 2015 we had approximately 50 VIBATIV sales representatives in the U.S. The risks of commercializing VIBATIV in the U.S. without a partner include:

costs and expenses associated with creating an independent sales and marketing organization with appropriate technical expertise and supporting infrastructure and distribution capability, including third party vendor logistics and consultant support, which costs and expenses could, depending on the scope and method of the marketing effort, exceed any product revenue from VIBATIV for several years;

our unproven ability to retain adequate numbers of effective sales and marketing personnel in the U.S.;

our unproven ability to retain medical science liaisons in the U.S. supporting physician education on the proper usage of VIBATIV;

the unproven ability of sales personnel to obtain access to and educate adequate numbers of physicians about prescribing VIBATIV in appropriate clinical situations;

the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

bearing the full costs of further U.S. development of telavancin.

If we are not successful in maintaining an internal sales and marketing organization with appropriate experience, technical expertise, supporting infrastructure, distribution capability and the ability to obtain access to and educate adequate numbers of physicians about prescribing VIBATIV in appropriate clinical situations, we will have difficulty commercializing VIBATIV in the U.S., which would adversely affect our business and financial condition and the price of our securities could fall. In the event we were to market, sell and distribute any additional products, we would face similar challenges and risks, which could adversely affect our business and financial condition and the price of our securities could fall.

Any delay in commencing or completing clinical studies for product candidates and any adverse results from clinical or non-clinical studies or regulatory obstacles product candidates may face, would harm our business and the price of our securities could fall.

Each of our product candidates must undergo extensive non-clinical and clinical studies as a condition to regulatory approval. Non-clinical and clinical studies are expensive, take many years to complete and study results may lead to delays in further studies or decisions to terminate programs. The commencement and completion of clinical studies for our product candidates may be delayed and programs may be terminated due to many factors, including, but not limited to:

lack of effectiveness of product candidates during clinical studies;

adverse events, safety issues or side effects relating to the product candidates or their formulation into medicines;

inability to raise additional capital in sufficient amounts to continue our development programs, which are very expensive;

inability to enter into partnering arrangements relating to the development and commercialization of our programs and product candidates;

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the need to sequence clinical studies as opposed to conducting them concomitantly in order to conserve resources;

our inability or the inability of our collaborators or licensees to manufacture or obtain from third parties materials sufficient for use in non-clinical and clinical studies;

governmental or regulatory delays and changes in regulatory requirements, policy and guidelines;

failure of our partners to advance our product candidates through clinical development;

delays in patient enrollment and variability in the number and types of patients available for clinical studies;

difficulty in maintaining contact with patients after treatment, resulting in incomplete data;

varying regulatory requirements or interpretations of data among the FDA and foreign regulatory authorities; and

a regional disturbance where we or our collaborative partners are enrolling patients in clinical trials, such as a pandemic, terrorist activities or war, political unrest or a natural disaster.

Our ongoing drug discovery and development efforts might not generate additional successful product candidates or approvable drugs.

Our compounds in clinical trials and our future leads for potential drug compounds are subject to the risks and failures inherent in the development of pharmaceutical products. These risks include, but are not limited to, the inherent difficulty in selecting the right drug and drug target and avoiding unwanted side effects, as well as unanticipated problems relating to product development, testing, enrollment, obtaining regulatory approvals, maintaining regulatory compliance, manufacturing, competition and costs and expenses that may exceed current estimates.

Clinical studies involving our product candidates may reveal that those candidates are ineffective, inferior to existing approved medicines, unacceptably toxic, or that they have other unacceptable side effects. In addition, the results of preclinical studies do not necessarily predict clinical success, and larger and later-stage clinical studies may not produce the same results as earlier-stage clinical studies.

Frequently, product candidates that have shown promising results in early preclinical or clinical studies have subsequently suffered significant setbacks or failed in later non-clinical or clinical studies. In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, varying levels of adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Clinical and non-clinical studies of product candidates often reveal that it is not possible or practical to continue development efforts for these product candidates. In addition, the design of a clinical trial can determine whether its results will support regulatory approval and flaws in the design of a clinical trial may not become apparent until the clinical trial is well underway. If our ongoing clinical studies for our current product candidates, such as the Phase 3 development program for revefenacin for the treatment of COPD and the earlier stage clinical studies for our gastrointestinal (GI)-targeted JAK inhibitor program or our NEP inhibitor program, are substantially delayed or fail to meet their designated end points we may not receive regulatory approval of any of these product candidates. In addition, our product candidates may have undesirable side effects or other unexpected characteristics that could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restricted label or the delay or denial of regulatory approval by regulatory authorities.

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If our product candidates are not approved by regulatory authorities, including the FDA, we will be unable to commercialize them.

The FDA must approve any new medicine before it can be marketed and sold in the U.S. We will not obtain this approval for a product candidate unless and until the FDA approves a new drug application ("NDA"). We, or our collaborative partners, must provide the FDA and similar foreign regulatory authorities with data from preclinical and clinical studies that demonstrate that our product candidates are safe and effective for a defined indication before they can be approved for commercial distribution. FDA or foreign regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. The processes by which regulatory approvals are obtained from the FDA and foreign regulatory authorities to market and sell a new product are complex, require a number of years, depend upon the type, complexity and novelty of the product candidate and involve the expenditure of substantial resources for research, development and testing. The FDA has substantial discretion in the drug approval process and may require us to conduct additional nonclinical and clinical testing or to perform post-marketing studies. Further, the implementation of new laws and regulations, and revisions to FDA clinical trial design guidance may lead to increased uncertainty regarding the approvability of new drugs. In addition, over the past decade, the FDA has implemented additional standards for approval of new drugs, including recommended advisory committee meetings for new molecular entities, and formal risk evaluation and mitigation requirements at the FDA's discretion. Even if we receive regulatory approval of a product, the approval may limit the indicated uses for which the drug may be marketed or impose significant restrictions or limitations on use of such product.

In addition, in order to market our medicines in foreign jurisdictions, we, or our collaborative partners, must obtain separate regulatory approvals in each country. The approval procedure varies among countries and can involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Conversely, failure to obtain approval in one or more jurisdictions may make approval in other jurisdictions more difficult. These laws, regulations, additional requirements and changes in interpretation could cause non-approval or further delays in the FDA's review and approval of our and our collaborative partner's product candidates, which would materially harm our business and financial condition and could cause the price of our securities to fall.

We rely on a single manufacturer for the Active Pharmaceutical Ingredient ("API") for telavancin and a separate, single manufacturer for VIBATIV drug product supply. Our business will be harmed if either of these single-source manufacturers are not able to satisfy demand and alternative sources are not available.

We have a single source of supply of API for telavancin and another, separate single source of supply of VIBATIV drug product. If, for any reason, either single-source third party manufacturer of telavancin API or of VIBATIV drug product is unable or unwilling to perform, or if its performance does not meet regulatory requirements, including maintaining current Good Manufacturing Practice ("cGMP") compliance, we may not be able to locate alternative manufacturers, enter into acceptable agreements with them or obtain sufficient quantities of API or finished drug product in a timely manner. Any inability to acquire sufficient quantities of API or finished drug product in a timely manner from current or future sources would adversely affect the commercialization of VIBATIV and our obligations to our partners and the price of our securities could fall.

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Our previous VIBATIV commercialization partner (at the time with Innoviva) failed to maintain a reliable source of drug product supply which resulted in critical product shortages and, eventually, suspension of commercialization for well over a year. We currently have an agreement with Hospira to supply VIBATIV drug product, which was entered into May 2012. In June 2013, the FDA approved Hospira as a VIBATIV drug product manufacturer, and this agreement with Hospira has been assigned to us. Although we believe that Hospira will continue to be a reliable supplier of VIBATIV drug product, if it cannot perform or if its performance does not meet regulatory requirements, including maintaining cGMP compliance, and if commercial manufacture of VIBATIV drug product cannot be arranged elsewhere on a timely basis, the commercialization of VIBATIV will be adversely affected. In addition, Pfizer acquired Hospira in 2015 and we cannot predict whether the acquisition will lead to changes in Hospira's operations which may adversely impact our single source of supply for VIBATIV drug product. We are currently in discussions with Hospira to extend the term of our agreement, which is currently set to expire at the end of 2017. Given the time required to locate and qualify another acceptable drug product manufacturer, any supply delay, suspension or cessation by Hospira (whether or not resulting from or related to the acquisition by Pfizer) would adversely affect the commercialization of VIBATIV and our obligations to our partners, which would adversely affect our business and financial condition and the price of our securities could fall.

We rely on a single source of supply for a number of our product candidates, and our business will be harmed if any of these single-source manufacturers are not able to satisfy demand and alternative sources are not available.

We have limited in-house production capabilities for preclinical and clinical study purposes, and depend primarily on a number of third-party API and drug product manufacturers. We may not have long-term agreements with these third parties and our agreements with these parties may be terminable at will by either party at any time. If, for any reason, these third parties are unable or unwilling to perform, or if their performance does not meet regulatory requirements, we may not be able to locate alternative manufacturers or enter into acceptable agreements with them. Any inability to acquire sufficient quantities of API and drug product in a timely manner from these third parties could delay preclinical and clinical studies and prevent us from developing our product candidates in a cost-effective manner or on a timely basis. In addition, manufacturers of our API and drug product are subject to the FDA's cGMP regulations and similar foreign standards and we do not have control over compliance with these regulations by our manufacturers.

Our manufacturing strategy presents the following additional risks:

because of the complex nature of many of our compounds, our manufacturers may not be able to successfully manufacture our APIs and/or drug products in a cost effective and/or timely manner and changing manufacturers for our APIs or drug products could involve lengthy technology transfer, validation and regulatory qualification activities for the new manufacturer;

the processes required to manufacture certain of our APIs and drug products are specialized and available only from a limited number of third-party manufacturers;

some of the manufacturing processes for our APIs and drug products have not been scaled to quantities needed for continued clinical studies or commercial sales, and delays in scale-up to commercial quantities could delay clinical studies, regulatory submissions and commercialization of our product candidates; and

because some of the third-party manufacturers are located outside of the U.S., there may be difficulties in importing our APIs and drug products or their components into the U.S. as a result of, among other things, FDA import inspections, incomplete or inaccurate import documentation or defective packaging.

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We are subject to extensive and ongoing regulation, oversight and other requirements by the FDA with respect to VIBATIV and failure to comply with these regulations and requirements may subject us to penalties that may adversely affect our financial condition or our ability to commercialize VIBATIV.

With VIBATIV approved in certain countries, we are subject to continuing regulatory obligations, such as safety reporting requirements and additional post-marketing obligations, including regulatory oversight of promotion and marketing. Prescription drug advertising and promotion are closely scrutinized by FDA, including substantiation of promotional claims, disclosure of risks and safety information, and the use of themes and imagery in advertising and promotional materials. As with all companies selling and marketing products regulated by the FDA in the U.S., we are prohibited from promoting any uses of VIBATIV that are outside the scope of use that has been expressly approved by FDA as safe and effective on the VIBATIV label. In September 2015, we announced that the FDA accepted for filing our supplemental NDA ("sNDA") to expand the VIBATIV label to include concurrent *Staphylococcus aureus* bacteremia. Under the Prescription Drug User Fee Act, the FDA has set a target of the second quarter of 2016 to complete its review of the sNDA, but there can be no assurance that the FDA will approve our sNDA or of the scope of any such approval if it is granted.

Furthermore, the U.S. labeling for VIBATIV contains a boxed warning. Products with boxed warnings are subject to more restrictive advertising regulations than products without such warnings and FDA regulations prohibit the use of reminder advertising for VIBATIV. In addition, the VIBATIV labeling for hospital-acquired and ventilator associated bacterial pneumonia ("HABP/VABP") in the U.S. and the European Union specifies that VIBATIV should be reserved for use when alternative treatments are not suitable. These restrictions add complexity to the marketing of VIBATIV.

The FDA has also required that we evaluate the safety of VIBATIV use during pregnancy by developing and maintaining a prospective, observational pregnancy exposure registry study conducted in the United States. This postmarketing study remains ongoing, and we are required to complete the study according to a timeframe agreed upon with FDA. The study's original projected completion date is the end of 2019. In addition, the FDA has required that we comply with a risk evaluation and mitigation strategy ("REMS") to inform healthcare providers and patients of key risks via a communication plan. Healthcare providers periodically receive letters reminding them of the major potential risks associated with VIBATIV and patients receive a medication guide with each course of antibiotic use. The healthcare provider letter is also available on the product website. The REMS stipulates that we make assessments of the efficacy of these educational efforts and provide reports to FDA at specified intervals.

In addition, the manufacturing, labeling, packaging, adverse event reporting, advertising, promotion and recordkeeping for the approved product remain subject to extensive and ongoing regulatory requirements. If we become aware of previously unknown problems with an approved product in the U.S. or overseas or at a contract manufacturer's facilities, a regulatory authority may impose restrictions on the product, the contract manufacturers or on us, including requiring us to reformulate the product, conduct additional clinical studies, change the labeling of the product, withdraw the product from the market or require the contract manufacturer to implement changes to its facilities.

We are also subject to regulation by regional, national, state and local agencies, including the Department of Justice, the Federal Trade Commission, the Office of Inspector General of the U.S. Department of Health and Human Services ("OIG") and other regulatory bodies with respect to VIBATIV, as well as governmental authorities in those foreign countries in which any of our product candidates are approved for commercialization. The Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and other federal and state statutes and regulations govern to varying degrees the research, development, manufacturing and commercial activities relating to prescription pharmaceutical products, including non-clinical and clinical testing, approval, production, labeling, sale, distribution, import, export, post-market surveillance, advertising, dissemination of information and promotion. If we

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or any third parties that provide these services for us are unable to comply, we may be subject to regulatory or civil actions or penalties that could significantly and adversely affect our business.

Regulatory approval for our product candidates, if any, may include similar or other limitations on the indicated uses for which we can market our medicines or the patient population that may utilize our medicines, which may limit the market for our medicines or put us at a competitive disadvantage relative to alternative therapies.

Any failure to maintain regulatory approval will limit our ability to commercialize VIBATIV or our product candidates and if we fail to comply with FDA regulations and requirements regarding VIBATIV or any of our product candidates, the FDA could potentially take a number of enforcement actions against us, including the issuance of untitled letters, warning letters, preventing the introduction or delivery of VIBATIV into interstate commerce in the United States, misbranding charges, product seizures, injunctions, and civil monetary penalties, which would materially and adversely affect our business and financial condition and may cause the price of our securities to fall.

The risks identified in this risk factor relating to regulatory actions and oversight by agencies in the U.S. and throughout the world also apply to the commercialization of any partnered products by our collaboration partners, and such regulatory actions and oversight may limit our collaboration partners' ability to commercialize such products, which could materially and adversely affect our business and financial condition, which may cause the price of our securities to fall.

We may face competition from companies seeking to market generic versions of VIBATIV.

For a discussion of the risk of generic competition to VIBATIV, please see the following risk factor below "If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively in our market."

If our partners do not satisfy their obligations under our agreements with them, or if they terminate our partnerships with them, we may not be able to develop or commercialize our partnered product candidates as planned.

We have an exclusive development and commercialization agreement with Alfa Wassermann for velusetrag, our lead compound in the 5-HT4 program, covering the European Union, Russia, China, Mexico and certain other countries. In October 2012, we (at the time with Innoviva) also entered into a research collaboration and license agreement with Merck & Co., Inc. ("Merck") to discover, develop and commercialize novel small molecule therapeutics for the treatment of cardiovascular disease, which Merck terminated in September 2013. We also have a commercialization agreement with Clinigen for VIBATIV in the European Union and certain other European countries (including Switzerland and Norway). In connection with these agreements, these parties have certain rights regarding the use of its patents and technology with respect to the compounds in our development programs, including development and marketing rights. The Alfa Wassermann and Clinigen agreements were assigned to us in the Spin-Off. The Alfa Wassermann agreement provides research and development funding for the program under license. In January 2015, we entered into a collaboration agreement with Mylan for the development and commercialization of a nebulized formulation of our LAMA revefenacin (TD-4208). Under the terms of the agreement, we and Mylan will co-develop nebulized revefenacin for COPD and other respiratory diseases.

Our partners might not fulfill all of their obligations under these agreements, and, in certain circumstances, they may terminate our partnership with them as Astellas did in January 2012 with its VIBATIV agreement and as Merck did in September 2013 with the cardiovascular disease collaboration. In either event, we may be unable to assume the development and commercialization of the product candidates covered by the agreements or enter into alternative arrangements with a third party to develop and commercialize such product candidates. If a partner elected to promote its own

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products and product candidates in preference to those licensed from us, the development and commercialization of product candidates covered by the agreements could be delayed or terminated, and future payments to us could be delayed, reduced or eliminated and our business and financial condition could be materially and adversely affected. Accordingly, our ability to receive any revenue from the product candidates covered by these agreements is dependent on the efforts of our partners. If a partner terminates or breaches its agreements with us, otherwise fails to complete its obligations in a timely manner or alleges that we have breached our contractual obligations under these agreements, the chances of successfully developing or commercializing product candidates under the collaboration could be materially and adversely affected. We could also become involved in disputes with a partner, which could lead to delays in or termination of our development and commercialization programs and time-consuming and expensive litigation or arbitration. Furthermore, termination of an agreement by a partner could have an adverse effect on the price of our ordinary shares or other securities even if not material to our business.

Because GSK is a strategic partner of Innoviva, a strategic partner of TRC and a significant shareholder of us, it may take actions that in certain cases are materially harmful to our business and to our other shareholders.

Based on our review of publicly available filings, as of March 31, 2016, GSK beneficially owned approximately 23.3% of our outstanding ordinary shares. GSK is also a strategic partner to Innoviva with rights and obligations under the strategic alliance agreement and under the collaboration agreement assigned to TRC (the "GSK-Innoviva Agreements") that may cause GSK's interests to differ from the interests of us and our other shareholders. In particular, if the Closed Triple or a MABA/ICS in either the U.S. or the European Union is approved, GSK's diligent efforts obligations under the GSK- Innoviva Agreements with regard to commercialization matters will have the objective of focusing on the best interests of patients and maximizing the net value of the overall portfolio of products under the GSK-Innoviva Agreements. Following such regulatory approval, GSK's commercialization efforts will be guided by a portfolio approach across products in which we have an indirect interest through TRC and products in which we have no interest. Accordingly, GSK's commercialization efforts may have the effect of reducing the value of our interest in TRC. Furthermore, GSK has a substantial respiratory product portfolio in addition to the products covered by the GSK-Innoviva Agreements. GSK may make respiratory product portfolio decisions or statements about its portfolio which may be, or may be perceived to be, harmful to the respiratory products partnered with Innoviva and TRC. For example, GSK could promote its own respiratory products and/or delay or terminate the development or commercialization of the respiratory programs covered by the GSK-Innoviva Agreements. Also, given the potential future royalty payments GSK may be obligated to pay under the GSK-Innoviva Agreements, GSK may seek to acquire us or acquire our interests in TRC in order to effectively reduce those payment obligations and the price at which GSK might seek to acquire us may not reflect our true value. Although the actions GSK may take to acquire us are limited under our governance agreement with GSK (the "Governance Agreement"), this agreement will expire on December 31, 2017. The timing of when GSK may seek to acquire us could potentially be when it possesses information regarding the status of drug programs covered by the GSK-Innoviva Agreements that has not been publicly disclosed and is not otherwise known to us. As a result of these differing interests, GSK may take actions that it believes are in its best interest but which might not be in the best interests of either us or our other shareholders. In addition, GSK could also seek to challenge our or Innoviva's post-Spin-Off operations as violating or allowing it to terminate the GSK-Innoviva Agreements, including by violating the confidentiality provisions of those agreements or the master agreement between GSK, Innoviva and us entered into in connection with the Spin-Off, or otherwise violating its legal rights. While we believe our operations fully comply with the GSK-Innoviva Agreements, the master agreement and applicable law, there can be no assurance that we or Innoviva will prevail against any such claims by GSK. Moreover, regardless of the merit of any claims by GSK,

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we may incur significant cost and diversion of resources in defending them. In addition, any other action or inaction by either GSK or Innoviva that results in a material dispute, allegation of breach, litigation, arbitration, or significant disagreement between those parties may be interpreted negatively by the market or by our investors, could harm our business and cause the price of our securities to fall. Examples of these kinds of issues include but are not limited to non-performance of contractual obligations and allegations of non-performance, disagreements over the relative marketing and sales efforts for Innoviva's partnered products and other GSK respiratory products, disputes over public statements, and similar matters. In general, any uncertainty about the respiratory programs partnered with GSK, the enforceability of the GSK-Innoviva Agreements or the relationship/partnership between Innoviva and GSK could result in significant reduction in the market price of our securities and other material harm to our business.

Agreements entered into with or for the benefit of GSK in connection with the Spin-Off may significantly restrict our business and affairs.

On March 3, 2014, in connection with the Spin-Off, we, Innoviva and GSK entered into a number of agreements that may significantly restrict our business and affairs. In particular, we, Innoviva and GSK entered into a three-way master agreement (the "Master Agreement") that, among other things, requires GSK's consent to make any changes to (A) the Separation and Distribution Agreement and ancillary agreements that would, individually or in the aggregate, reasonably be expected to adversely affect GSK in any material respect or (B) the TRC Limited Liability Company Agreement, which consent is not to be unreasonably withheld, conditioned or delayed, provided that GSK may withhold, condition or delay such consent in its sole discretion with respect to certain sections of the TRC Limited Liability Company Agreement and any changes to the governance structure of TRC, the confidentiality restrictions, the consent rights, and the transfer restrictions in the TRC Limited Liability Company Agreement. We and GSK also entered into (i) the Governance Agreement that, among other things, provides share purchase rights to GSK and exempts GSK from triggering our Rights Agreement until December 31, 2017, (ii) a registration rights agreement that gives GSK certain registration rights with respect to our ordinary shares held by GSK and (iii) an extension agreement that extends to us certain restrictive covenants similar to those applicable to Innoviva under the GSK-Innoviva Agreements. There can be no assurance that these restrictions will not materially harm our business, particularly given that GSK's interests may not be aligned with the interests of our business or our other shareholders.

We depend on third parties in the conduct of our clinical studies for our product candidates.

We depend on independent clinical investigators, contract research organizations and other third-party service providers in the conduct of our non-clinical and clinical studies for our product candidates. We rely heavily on these parties for execution of our non-clinical and clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that our clinical studies are conducted in accordance with good clinical practices ("GCPs") and other regulations as required by the FDA and foreign regulatory authorities, and the applicable protocol. Failure by these parties to comply with applicable regulations, GCPs and protocols in conducting studies of our product candidates can result in a delay in our development programs or non-approval of our product candidates by regulatory authorities.

The FDA, and equivalent authorities in other countries, enforces GCPs and other regulations through periodic inspections of trial sponsors, clinical research organizations ("CROs"), principal investigators and trial sites. If we or any of the third parties on which we have relied to conduct our clinical studies are determined to have failed to comply with GCPs (or other equivalent regulations outside the United States), the study protocol or applicable regulations, the clinical data generated in our studies may be deemed unreliable. This could result in non-approval of our product candidates by

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the FDA, or equivalent authorities in other countries, or we, the FDA, or equivalent authorities in other countries may decide to conduct additional audits or require additional clinical studies, which would delay our development programs, could result in significant additional costs and the price of our securities could fall.

We face substantial competition from companies with more resources and experience than we have, which may result in others discovering, developing, receiving approval for or commercializing products before or more successfully than we do.

Our ability to succeed in the future depends on our ability to demonstrate and maintain a competitive advantage with respect to our approach to the discovery, development and commercialization of medicines. Our objective is to discover, develop and commercialize new small molecule medicines with superior efficacy, convenience, tolerability and/or safety using our proprietary insight in chemistry, biology and multivalency, where applicable. We expect that any medicines that we commercialize with or without our collaborative partners will compete with existing or future market-leading medicines.

Many of our current and potential competitors have substantially greater financial, technical and personnel resources than we have. In addition, many of these competitors have significantly greater commercial infrastructures than we have. Our ability to compete successfully will depend largely on our ability to leverage our experience in drug discovery and development, and, more recently, commercialization, to:

discover and develop medicines that are superior to other products in the market;

attract and retain qualified personnel;

obtain patent and/or other proprietary protection for our medicines and technologies;

obtain required regulatory approvals;

develop and effectively implement commercialization strategies, with or without collaborative partners; and

successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicines.

Pharmaceutical companies, including companies with which we collaborate, may invest heavily to quickly discover and develop or in-license novel compounds that could make our product candidates obsolete. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA or equivalent regulatory approval outside the United States or discovering, developing and commercializing medicines before we do. Other companies are engaged in the discovery of medicines that would compete with the product candidates that we are developing.

Any new medicine that competes with a generic or proprietary market leading medicine must demonstrate compelling advantages in efficacy, convenience, tolerability and/or safety in order to overcome severe price competition and be commercially successful. VIBATIV must demonstrate these advantages in certain circumstances, as it competes with vancomycin and linezolid, relatively inexpensive generic drugs that are manufactured by a number of companies, and a number of existing antibacterial drugs marketed by major and other pharmaceutical companies. In addition, sales of a generic version of daptomycin could begin in 2016. If we are not able to compete effectively against our current and future competitors, our business will not grow, our financial condition and operations will suffer and the price of our securities could fall.

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Certain of our directors and officers may have actual or potential conflicts of interest because of their equity ownership in Innoviva, which actual or potential conflicts may harm our business, prospects and financial condition and result in the diversion of corporate opportunities to Innoviva.

Certain of our directors and executive officers hold shares of Innoviva's common stock or rights to acquire such shares, and these holdings may be significant for some of these individuals compared to their total assets. This ownership of Innoviva common stock by our officers and most of our directors may create, or may create the appearance of, conflicts of interest when these directors and officers are faced with decisions that could have different implications for Innoviva and for us. For example, potential or actual conflicts could arise relating to: our relationship with Innoviva, including Innoviva's and our respective rights and obligations under agreements entered into in connection with the Spin-Off; Innoviva's management of TRC, particularly given that we and Innoviva have different economic interests in TRC; and corporate opportunities that may be available to both companies in the future. Although we and Innoviva have implemented policies and procedures to identify and properly address such potential and actual conflicts of interest, there can be no assurance that, when such conflicts are resolved in accordance with applicable laws, such conflicts of interest will not harm our business, prospects and financial condition and result in the diversion of corporate opportunities to Innoviva.

If we lose key management or scientific personnel, or if we fail to attract and retain key employees, our ability to discover and develop our product candidates and commercialize VIBATIV and any other products that may be approved in the future will be impaired.

We are highly dependent on principal members of our management team and scientific staff, and in particular, our Chief Executive Officer, Rick E Winningham, to operate our business. Mr. Winningham has significant pharmaceutical industry experience. The loss of Mr. Winningham's services could impair our ability to discover, develop and commercialize new medicines.

If we fail to retain our qualified personnel or replace them when they leave, we may be unable to continue our discovery, development and commercialization activities, which may cause the price of our securities to fall. In addition, our U.S. operating subsidiary's facility and most of its employees are located in northern California, headquarters to many other biotechnology and biopharmaceutical companies and many academic and research institutions. As a result, competition for certain skilled personnel in our market is intense. None of our employees have employment commitments for any fixed period of time and they all may leave our employment at will. If we fail to retain our qualified personnel or replace them when they leave, we may be unable to continue our development and commercialization activities and the price of our securities could fall.

Our business and operations would suffer in the event of significant disruptions of information technology systems or security breaches.

We rely extensively on computer systems to maintain information and manage our finances and business. In the ordinary course of business, we collect, store and transmit large amounts of confidential information (including but not limited to trade secrets or other intellectual property, proprietary business information and personal information) and it is critical that we maintain the confidentiality and integrity of such confidential information. Although we have security measures in place, our internal information technology systems and those of our CROs and other service providers are vulnerable to service interruptions and security breaches from inadvertent or intentional actions by our employees, service providers and/or business partners, from cyber-attacks by malicious third parties, and/or from, natural disasters, terrorism, war and telecommunication and electrical failures. Cyber-attacks are increasing in their frequency, sophistication, and intensity, and have become increasingly difficult to detect. Significant disruptions of information technology systems or security breaches could adversely affect our business operations and result in financial, legal, business and reputational harm to

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us, including significant liability and/or significant disruption to our business. If a disruption of information technology systems or security breach results in a loss of or damage to our data or regulatory applications, unauthorized access, use, or disclosure of, or the prevention of access to, confidential information, or other harm to our business, we could incur liability and reputational harm, we could be required to comply with federal and/or state breach notification laws and foreign law equivalents, the further development of our product candidates could be delayed and the price of our securities could fall. For example, the loss of clinical trial data from completed or ongoing clinical trials of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Although we have security and fraud prevention measures in place, we have been subject to immaterial payment fraud activity. Moreover, there can be no assurance that such security measures will prevent service interruptions or security breaches that could adversely affect our business.

Our U.S. operating subsidiary's facility is located near known earthquake fault zones, and the occurrence of an earthquake, extremist attack or other catastrophic disaster could cause damage to our facilities and equipment, which could require us to cease or curtail operations.

Our U.S. operating subsidiary's facility is located in the San Francisco Bay Area near known earthquake fault zones and therefore will be vulnerable to damage from earthquakes. In October 1989, a major earthquake struck this area and caused significant property damage and a number of fatalities. We are also vulnerable to damage from other types of disasters, including power loss, attacks from extremist organizations, fire, floods, communications failures and similar events. If any disaster were to occur, our ability to operate our business could be seriously impaired. In addition, the unique nature of our research activities and of much of our equipment could make it difficult for us to recover from this type of disaster. We may not have adequate insurance to cover our losses resulting from disasters or other similar significant business interruptions and we do not plan to purchase additional insurance to cover such losses due to the cost of obtaining such coverage. Any significant losses that are not recoverable under our insurance policies could seriously impair our business and financial condition, which could cause the price of our securities to fall.

We are an "emerging growth company" and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our ordinary shares less attractive to investors.

We are an "emerging growth company" under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. Where appropriate, we plan to avail ourselves of this exemption from new or revised accounting standards and, therefore, we may not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

For as long as we continue to be an emerging growth company, we also intend to take advantage of certain other exemptions from various reporting requirements that are applicable to other public companies including, but not limited to, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, exemptions from the requirements of holding a nonbinding advisory shareholder vote on executive compensation and any golden parachute payments not previously approved, exemption from the requirement of auditor attestation in the assessment of our internal control over financial reporting and exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis). Therefore, the information that we intend to provide shareholders will be different than what is available with respect to some other public companies. We cannot predict if investors will find our ordinary shares less attractive because we rely

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on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may be more volatile.

We were an emerging growth company for all of 2015 and will remain an emerging growth company until the earliest of (i) the end of the fiscal year in which the market value of our ordinary shares that is held by non-affiliates exceeds \$700 million as of the end of the second fiscal quarter, (ii) the end of the fiscal year in which we have total annual gross revenues of \$1 billion or more during such fiscal year, (iii) the date on which we issue more than \$1 billion in non-convertible debt in a three-year period or (iv) December 31, 2019, the end of the fiscal year following the fifth anniversary of the date of the first sale of our ordinary shares pursuant to an effective registration statement filed under the Securities Act.

Our historical financial information prior to the Spin-Off may not reflect what our financial position, results of operations or cash flows would have been as a stand-alone company during the periods presented and is not necessarily indicative of our future financial position, future results of operations or future cash flows.

Our historical financial information prior to the Spin-Off does not necessarily reflect what our financial position, results of operations or cash flows would have been as a stand-alone company during the periods presented and is not necessarily indicative of our future financial position, future results of operations or future cash flows. This is primarily a result of the following factors:

prior to the Spin-Off, our business was operated by Innoviva as part of its broader corporate organization rather than as a stand-alone company, and our business was able to leverage Innoviva's financial resources and creditworthiness;

prior to the Spin-Off, certain general administrative functions were performed by Innoviva for the combined entity. Our historical consolidated financial statements reflect allocations of costs for services shared with Innoviva. These allocations may differ from the costs we will incur for these services as an independent company;

holding other factors constant, our cost of capital as a stand-alone company is likely higher on average than Innoviva's cost of capital was as a combined business prior to the Spin-Off;

following the Spin-Off, we are responsible for the additional costs associated with being an independent, public company, including costs related to corporate governance and listed and registered securities; and

having separated from Innoviva, there is a risk that we may be more susceptible to market fluctuations and other adverse events than we would have been were we still a part of Innoviva.

Our accounting and other management systems and resources may not be adequately prepared to meet the financial reporting and other requirements to which we became subject following the Spin-Off. If we are unable to achieve and maintain effective internal controls, our business, financial position and results of operations could be adversely affected.

We are subject to the reporting and other obligations under the Exchange Act, including the requirements of Section 404 of the Sarbanes-Oxley Act of 2002, which will require annual management assessments of the effectiveness of our internal control over financial reporting. When and if we become a "large accelerated filer" and are no longer an "emerging growth company," each as defined in the Exchange Act, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. These reporting and other obligations will place significant demands on our management and administrative and operational resources, including accounting resources.

In addition, we are currently replacing our existing enterprise resource planning ("ERP") software system. Our ERP system is critical to our ability to accurately maintain books and records, record

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transactions, provide important information to our management and prepare our financial statements. Such an implementation is complex and difficult and will require us to address a number of challenges including data conversion, system cutover and user training. As a result, it represents a major undertaking financially and from a management and personnel perspective. Our business and results of operations may be adversely affected if we experience operating problems and/or cost overruns during the ERP implementation process, or if the ERP system and the associated process changes do not give rise to the benefits that we expect. Additionally, if we do not effectively implement the ERP system as planned or if the system does not operate as intended, it could be disruptive and adversely affect our operations and results of operations, including our ability to report accurate and timely financial results and the effectiveness of our internal control over financial reporting.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States. Any failure to achieve and maintain effective internal controls could have an adverse effect on our business, financial position and results of operations.

We have only been operating as a stand-alone entity since June 2, 2014 and therefore we have a limited history operating as an independent company upon which you can evaluate us.

We have only been operating as a stand-alone entity since June 2, 2014 and therefore we have a limited operating history as an independent company upon which you can evaluate us. While our biopharmaceutical business has constituted a substantial part of the historic operations of Innoviva, we did not operate as a stand-alone company without the right to receive potential royalty revenue derived from Innoviva's GSK Partnered Respiratory Program (the "Royalty Business") until the Spin-Off. As a new independent company, our ability to satisfy our obligations and achieve profitability will be primarily dependent upon the future performance of our biopharmaceutical business, and we do not rely upon the revenues, capital resources and cash flows of the Royalty Business remaining with Innoviva.

We may be treated as a U.S. corporation for U.S. federal income tax purposes.

For U.S. federal income tax purposes, a corporation generally is considered tax resident in the place of its incorporation. Theravance Biopharma is incorporated under Cayman Islands law and established tax residency in Ireland effective July 1, 2015. Therefore, it should be a non-U.S. corporation under this general rule. However, Section 7874 of the Internal Revenue Code of 1986, as amended (the "Code"), contains rules that may result in a foreign corporation being treated as a U.S. corporation for U.S. federal income tax purposes. The application of these rules is complex and there is little guidance regarding certain aspects of their application.

Under Section 7874 of the Code, a corporation created or organized outside the U.S. will be treated as a U.S. corporation for U.S. federal tax purposes if (i) the foreign corporation directly or indirectly acquires substantially all of the properties held directly or indirectly by a U.S. corporation, (ii) the former shareholders of the acquired U.S. corporation hold at least 80% of the vote or value of the shares of the foreign acquiring corporation by reason of holding stock in the U.S. acquired corporation, and (iii) the foreign corporation's "expanded affiliated group" does not have "substantial business activities" in the foreign corporation's country of incorporation relative to its expanded affiliated group's worldwide activities. For this purpose, "expanded affiliated group" generally means the foreign corporation and all subsidiaries in which the foreign corporation, directly or indirectly, owns more than 50% of the stock by vote and value, and "substantial business activities" generally means at least 25% of employees (by number and compensation), assets and gross income of our expanded affiliated group are based, located and derived, respectively, in the country of incorporation.

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We do not expect to be treated as a U.S. corporation under Section 7874 of the Code, because we do not believe that the assets contributed to us by Innoviva constituted "substantially all" of the properties of Innoviva (as determined on both a gross and net fair market value basis). However, the Internal Revenue Service ("IRS") may disagree with our conclusion on this point and assert that, in its view, the assets contributed to us by Innoviva did constitute "substantially all" of the properties of Innoviva. In addition, there could be legislative proposals to expand the scope of U.S. corporate tax residence and there could be changes to Section 7874 of the Code or the Treasury Regulations promulgated thereunder that could apply retroactively and could result in Theravance Biopharma being treated as a U.S. corporation.

If it were determined that we should be treated as a U.S. corporation for U.S. federal income tax purposes, we could be liable for substantial additional U.S. federal income tax on our post-Spin-Off taxable income. In addition, payments of dividends to non-U.S. holders may be subject to U.S. withholding tax.

Taxing authorities may challenge our structure and transfer pricing arrangements.

We are incorporated in the Cayman Islands, maintain subsidiaries in the Cayman Islands, United States, the United Kingdom and Ireland, and effective July 1, 2015, we migrated our tax residency from the Cayman Islands to Ireland. Due to economic and political conditions various countries are actively considering changes to existing tax laws. We cannot predict the form or timing of potential legislative changes that could have a material adverse impact on our results of operations. In addition, significant judgment is required in determining our worldwide provision for income taxes. Various factors may have favorable or unfavorable effects on our income tax rate including, but not limited to the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions such as the Cayman Islands and Ireland, together with intra-group transfer pricing agreements. Taxing authorities may challenge our structure and transfer pricing arrangements through an audit or lawsuit. Responding to or defending such a challenge could be expensive and consume time and other resources, and divert management's time and focus from operating our business. We cannot predict whether taxing authorities will conduct an audit or file a lawsuit challenging this structure, the cost involved in responding to any such audit or lawsuit, or the outcome. We may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future which could result in reduced cash flows and have a material adverse effect on our business, financial condition and growth prospects.

If we are required to indemnify Innoviva, or if we are not able to collect on indemnification rights from Innoviva, our business prospects and financial condition may be harmed.

We agreed to indemnify Innoviva from and after the Spin-Off with respect to (i) all debts, liabilities and obligations transferred to us in connection with the Spin-Off (including our failure to pay, perform or otherwise promptly discharge any such debts, liabilities or obligations after the Spin-Off), (ii) any misstatement or omission of a material fact resulting in a misleading statement in our Information Statement distributed to Innoviva stockholders in connection with the Spin-Off and (iii) any breach by us of certain agreements entered into with Innoviva in connection with the Spin-Off (namely, the Separation and Distribution Agreement, the Transition Services Agreement, the Employee Matters Agreement, the Tax Matters Agreement, and the Facility Sublease Agreement). We are not aware of any existing indemnification obligations at this time, but any such indemnification obligations that may arise could be significant. Under the terms of the Separation and Distribution Agreement, Innoviva agreed to indemnify us from and after the Spin-Off with respect to (i) all debts, liabilities and obligations retained by Innoviva after the Spin-Off (including its failure to pay, perform or otherwise promptly discharge any such debts, liabilities or obligations after the Spin-Off) and (ii) any breach by Innoviva of the Separation and Distribution Agreement, the Transition Services Agreement, the

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Employee Matters Agreement, the Tax Matters Agreement, and the Facility Sublease Agreement. Our and Innoviva's ability to satisfy these indemnities, if called upon to do so, will depend upon our and Innoviva's future financial strength. If we are required to indemnify Innoviva, or if we are not able to collect on indemnification rights from Innoviva, our business prospects and financial condition may be harmed.

RISKS RELATED TO LEGAL AND REGULATORY UNCERTAINTY

If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, patent applications, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. Any involuntary disclosure to or misappropriation by third parties of this proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. The status of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and is very uncertain. As of March 31, 2016, we or one of our wholly-owned subsidiaries owned 426 issued United States patents and 1,585 granted foreign patents, as well as additional pending United States and foreign patent applications. Our patent applications may be challenged or fail to result in issued patents and our existing or future patents may be invalidated or be too narrow to prevent third parties from developing or designing around these patents. If the sufficiency of the breadth or strength of protection provided by our patents with respect to a product candidate is threatened, it could dissuade companies from collaborating with us to develop product candidates and threaten our ability to commercialize products. Further, if we encounter delays in our clinical trials or in obtaining regulatory approval of our product candidates, the patent lives of the related product candidates would be reduced.

In addition, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, for processes for which patents are difficult to enforce and for any other elements of our drug discovery and development processes that involve proprietary know-how, information and technology that is not covered by patent applications. Although we require our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information and technology to enter into confidentiality agreements, we cannot be certain that this know-how, information and technology will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Further, the laws of some foreign countries do not protect proprietary rights to the same extent as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or, if established, maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition and results of operations, which could cause the price of our securities to fall.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, a company may submit an abbreviated new drug application ("ANDA") under section 505(j) of the Federal Food, Drug, and Cosmetic Act to market a generic version of an approved drug. Because a generic applicant does not conduct its own clinical studies, but instead relies on the FDA's finding of safety and effectiveness for the approved drug, it is able to introduce a competing product into the market at a cost significantly below that of the original drug. Although we have multiple patents protecting VIBATIV until at least 2021 the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, generic applicants could potentially submit "paragraph IV certifications" to FDA stating that such patents are invalid or will not be infringed by the applicant's product. We have not received any such paragraph IV notifications but if any competitors successfully

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challenge our patents, we would face substantial competition. If we are not able to compete effectively against such future competition, our business will not grow, our financial condition and operations will suffer and the price of our securities could fall.

Litigation or third-party claims of intellectual property infringement would require us to divert resources and may prevent or delay our drug discovery and development efforts.

Our commercial success depends in part on us and our partners not infringing the patents and proprietary rights of third parties. Third parties may assert that we or our partners are using their proprietary rights without authorization. There are third party patents that may cover materials or methods for treatment related to our product candidates. At present, we are not aware of any patent infringement claims with merit that would adversely and materially affect our ability to develop our product candidates, but nevertheless the possibility of third party allegations cannot be ruled out. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Furthermore, parties making claims against us or our partners may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense against these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

In the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties or pay royalties. In addition, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. In addition, in the future we could be required to initiate litigation to enforce our proprietary rights against infringement by third parties. Prosecution of these claims to enforce our rights against others would involve substantial litigation expenses and divert substantial employee resources from our business. If we fail to effectively enforce our proprietary rights against others, our business will be harmed and the price of our securities could fall.

If the efforts of our partners or future partners to protect the proprietary nature of the intellectual property related to collaboration assets are not adequate, the future commercialization of any medicines resulting from collaborations could be delayed or prevented, which would materially harm our business and could cause the price of our securities to fall.

The risks identified in the two preceding risk factors may also apply to the intellectual property protection efforts of our partners or future partners and to GSK with respect to the GSK-Partnered Respiratory Programs in which we hold an economic interest. To the extent the intellectual property protection of any partnered assets are successfully challenged or encounter problems with the United States Patent and Trademark Office or other comparable agencies throughout the world, the future commercialization of these potential medicines could be delayed or prevented. Any challenge to the intellectual property protection of a late-stage development asset, particularly those of the GSK-Partnered Respiratory Programs in which we hold an economic interest, could harm our business and cause the price of our securities to fall.

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Product liability lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our medicines.

The risk that we may be sued on product liability claims is inherent in the development and commercialization of pharmaceutical products and have likely increased with the commercial reintroduction of VIBATIV. Side effects of, or manufacturing defects in, products that we or our partners develop or commercialize could result in the deterioration of a patient's condition, injury or even death. The VIBATIV prescribing information describes several potential adverse effects observed during clinical trials, including increased mortality versus vancomycin in patients with HABP/VABP who had pre-existing moderate to severe renal impairment, decreased clinical response in patients with cSSSI who had pre-existing moderate/severe renal impairment, and other renal adverse events. The prescribing information includes a black box warning regarding increased mortality in patients with pre-existing moderate/severe renal impairment who were treated with VIBATIV for HABP/VABP, new onset or worsening renal impairment, use in women of childbearing potential or during pregnancy and adverse developmental outcomes observed in 3 animal species. Once a product is approved for sale and commercialized, the likelihood of product liability lawsuits tends to increase. Claims may be brought by individuals seeking relief for themselves or by individuals or groups seeking to represent a class, asserting injuries based both on potential adverse effects described in the label as well as adverse events not yet observed. Also, changes in laws outside the U.S. are expanding our potential liability for injuries that occur during clinical trials. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and may be forced to limit or forgo further commercialization of the applicable products.

Although we maintain general liability and product liability insurance, this insurance may not fully cover potential liabilities and we cannot be sure that our insurer will not disclaim coverage as to a future claim. In addition, inability to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims could prevent or inhibit the commercial production and sale of our products, which could adversely affect our business. The cost of defending any product liability litigation or other proceeding, even if resolved in our favor, could be substantial and uncertainties resulting from the initiation and continuation of product liability litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Product liability claims could also harm our reputation, which may adversely affect our and our partners' ability to commercialize our products successfully and the price of our securities could fall.

Changes in healthcare law and implementing regulations, including government restrictions on pricing and reimbursement, as well as healthcare policy and other healthcare payor cost-containment initiatives, may negatively impact our ability to generate revenues.

The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care costs to contain or reduce costs of health care may adversely affect one or more of the following:

our or our collaborators' ability to set and collect a price we believe is reasonable for our product;

our ability to generate revenues and achieve profitability; and

the availability of capital.

The pricing and reimbursement environment for VIBATIV and any future products may change in the future and become more challenging due to, among other reasons, policies advanced by the current or any new presidential administration, federal agencies, new healthcare legislation passed by Congress or fiscal challenges faced by all levels of government health administration authorities. Among policy

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makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of VIBATIV and other products we may bring to market, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (together the "Healthcare Reform Act"), is a sweeping measure intended to expand healthcare coverage within the United States, primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program. This law substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The Healthcare Reform Act contains a number of provisions that impact our business and operations. Changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, benefits for patients within a coverage gap in the Medicare Part D prescription drug program (commonly known as the "donut hole"), rules regarding prescription drug benefits under the health insurance exchanges, changes to the Medicare Drug Rebate program, expansion of the Public Health Service's 340B drug pricing discount program, fraud and abuse and enforcement. These changes will impact existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program.

Details of the changes to the Medicaid Drug Rebate program and the 340B program are discussed below under the risk factor " *If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.*" In particular, on February 1, 2016, the Centers for Medicare and Medicaid Services ("CMS"), the federal agency that administers the Medicare and Medicaid programs, issued final regulations to implement the changes to the Medicaid Drug Rebate program under the Healthcare Reform Act. These regulations became effective on April 1, 2016. We are evaluating the impact of these regulations on our business and operations. Congress could enact additional legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the Medicaid Drug Rebate program. The issuance of regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program has and will continue to increase our costs and the complexity of compliance, has been and will be time-consuming, and could have a material adverse effect on our results of operations.

Some states have elected not to expand their Medicaid programs by raising the income limit to 133% of the federal poverty level, as is permitted under the Healthcare Reform Act. For each state that does not choose to expand its Medicaid program, there may be fewer insured patients overall, which could impact our sales, business and financial condition. Where Medicaid patients receive insurance coverage under any of the new options made available through the Healthcare Reform Act, manufacturers may be required to pay Medicaid rebates on drugs used under these circumstances, which could impact manufacturer revenues. In addition, the federal government has also announced delays in the implementation of key provisions of the Healthcare Reform Act. The implications of these delays for our sales, business and financial condition, if any, are not yet clear.

Moreover, legislative changes to the Healthcare Reform Act remain possible. We expect that the Healthcare Reform Act, as currently enacted or as it may be amended in the future, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on

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our industry generally and on our ability to maintain or increase sales of our existing products or to successfully commercialize our product candidates, if approved.

Beginning on April 1, 2013, Medicare payments for all items and services under Part A and B, including drugs and biologicals, were reduced by 2% under the sequestration (i.e., automatic spending reductions) as required by federal law, which requires sequestration for most federal programs, excluding Medicaid, Social Security, and certain other programs. The law caps the cuts to Medicare payments for items and services at 2% and this will continue to 2025. As long as these cuts remain in effect, they could adversely impact payment for VIBATIV and our product candidates. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in and have certain price reporting obligations to the Medicaid Drug Rebate program and other governmental pricing programs, and we have obligations to report average sales price under the Medicare program.

Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions.

The Healthcare Reform Act made significant changes to the Medicaid Drug Rebate program, such as expanding rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well and changing the definition of average manufacturer price. The Healthcare Reform Act also increased the minimum Medicaid rebate; changed the calculation of the rebate for certain innovator products that qualify as line extensions of existing drugs; and capped the total rebate amount for innovator drugs at 100% of the average manufacturer price. Finally, the Healthcare Reform Act requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government.

On February 1, 2016, CMS issued final regulations to implement the changes to the Medicaid Drug Rebate program under the Healthcare Reform Act. These regulations became effective on April 1, 2016. We are evaluating the impact of these regulations on our business and operations. The issuance of regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program has and will continue to increase our costs and the complexity of compliance, has been and will be time-consuming, and could have a material adverse effect on our results of operations.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge no more than the 340B "ceiling price" for the

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manufacturer's covered outpatient drugs to a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The Healthcare Reform Act expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program. Changes to the definition of average manufacturer price and the Medicaid rebate amount under the Healthcare Reform Act and CMS's final regulations implementing those changes also could affect our 340B ceiling price calculations and negatively impact our results of operations.

The Healthcare Reform Act obligates the Secretary of the HHS to create regulations and processes to improve the integrity of the 340B program and to update the agreement that manufacturers must sign to participate in the 340B program to obligate a manufacturer to offer the 340B price to covered entities if the manufacturer makes the drug available to any other purchaser at any price and to report to the government the ceiling prices for its drugs. Health Resources and Services Administration ("HRSA") recently issued a proposed regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, as well as proposed omnibus guidance that addresses many aspects of the 340B program. HRSA is expected to issue additional proposed regulations in 2016. Any final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting.

Federal law also requires that a company that participates in the Medicaid Drug Rebate program report average sales price information each quarter to CMS for certain categories of drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Statutory or regulatory changes or CMS binding guidance could affect the average sales price calculations for our products and the resulting Medicare payment rate, and could negatively impact our results of operations. Also, the Medicare Part B drug payment methodology is subject to change based on potential demonstration projects undertaken by CMS or potential legislation enacted by Congress. For example, in March 2016, CMS proposed to conduct a demonstration project that would reduce the Medicare payment rates for most Part B drugs from average sales price plus 6% to average sales price plus 2.5% plus \$16.80 per drug per day for approximately half of the country. CMS indicated that it intends to implement this project in 2016, followed by a second phase of the demonstration in 2017 that would apply "value-based purchasing" tools to make further adjustments to payment rates. A final decision on this proposal is expected later this year.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B drug discount program.

We are liable for errors associated with our submission of pricing data. In addition to retroactive rebates and the potential for 340B program refunds, if we are found to have knowingly submitted any

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false price information to the government, we may be liable for civil monetary penalties in the amount of \$100,000 per item of false information. If we are found to have made a misrepresentation in the reporting of our average sales price, the Medicare statute provides for civil monetary penalties of up to \$10,000 for each misrepresentation for each day in which the misrepresentation was applied. Our failure to submit the required price data on a timely basis could result in a civil monetary penalty of \$10,000 per day for each day the information is late beyond the due date. Such failure also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program. In the event that CMS terminates our rebate agreement, federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs.

CMS and the OIG have pursued manufacturers that were alleged to have failed to report these data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot assure you that our submissions will not be found by CMS to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the VA, Department of Defense, Public Health Service, and Coast Guard and certain federal grantees, we are required to participate in the Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program, established by Section 603 of the Veterans Health Care Act of 1992. Under this program, we are obligated to make VIBATIV available for procurement on an FSS contract and charge a price that is no higher than the statutory Federal Ceiling Price ("FCP"). The FCP is based on the non-federal average manufacturer price ("Non-FAMP"), which we calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to penalties of \$100,000 for each item of false information. These obligations also contain extensive disclosure and certification requirements.

Under Section 703 of the National Defense Authorization Act for FY 2008, we are also required to pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. If we overcharge the government in connection with the FSS contract or Tricare Retail Pharmacy Program, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

If we fail to comply with data protection laws and regulations, we could be subject to government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity, which could negatively affect our operating results and business.

We are subject to data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the U.S., numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure, and protection of health-related and other personal information. Failure to comply with data protection laws and regulations could result in government enforcement actions (which could include civil and/or criminal penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business. In addition, we may obtain health information from third parties (e.g., healthcare providers who prescribe our products) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information

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Technology for Economic and Clinical Health Act ("HIPAA"). Although we are not directly subject to HIPAA other than potentially with respect to providing certain employee benefits we could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. HIPAA generally requires that healthcare providers and other covered entities obtain written authorizations from patients prior to disclosing protected health information of the patient (unless an exception to the authorization requirement applies). If authorization is required and the patient fails to execute an authorization or the authorization fails to contain all required provisions, then we may not be allowed access to and use of the patient's information and our research efforts could be impaired or delayed. Furthermore, use of protected health information that is provided to us pursuant to a valid patient authorization is subject to the limits set forth in the authorization (e.g., for use in research and in submissions to regulatory authorities for product approvals). In addition, HIPAA does not replace federal, state, international or other laws that may grant individuals even greater privacy protections.

EU member states and other jurisdictions where we operate have adopted data protection laws and regulations, which impose significant compliance obligations. For example, the EU Data Protection Directive imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. Switzerland has adopted similar restrictions. Data protection authorities from the different EU member states may interpret the applicable laws differently, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data in the EU. Although there are legal mechanisms to allow for the transfer of personal data from the EEA to the U.S., a recent decision of the European Court of Justice in the *Schrems* case (Case C-362/14 Maximilian Schrems v. Data Protection Commissioner) that invalidated the safe harbor framework has increased uncertainty around compliance with EU privacy law requirements. As a result of the decision, it is no longer possible to rely on safe harbor certification as a legal basis for the transfer of personal data from the EU to entities in the U.S. On February 29, 2016, the European Commission announced an agreement with the United States Department of Commerce ("DOC") to replace the invalidated Safe Harbor framework with a new EU-U.S. "Privacy Shield". The Privacy Shield is intended to address the requirements set out by the European Court of Justice in its recent ruling by imposing more stringent obligations on companies, providing stronger monitoring and enforcement by the DOC and Federal Trade Commission, and making commitments on the part of public authorities regarding access to information. However, the Privacy Shield is still not yet in effect. Related details are currently under review by the EU's Article 29 Working Party, an independent body established by the European Commission to provide guidance on the implementation of the EU Data Protection legislation. The Working Party is expected to render a non-binding opinion within the next few months. Taking that opinion into account, the European Commission is then expected to formally vote on the adequacy of the Privacy Shield program, at which point it will take effect. If we or our vendors fail to comply with applicable data privacy laws, or if the legal mechanisms we or our vendors rely upon to allow for the transfer of personal data from the EEA or Switzerland to the U.S. (or other countries not considered by the European Commission to provide an adequate level of data protection) are not considered adequate, we could be subject to government enforcement actions and significant penalties against us, and our business could be adversely impacted if our ability to transfer personal data outside of the EEA or Switzerland is restricted, which could adversely impact our operating results. In December 2015, a proposal for an EU General Data Protection Regulation, intended to replace the current EU Data Protection Directive, was agreed between the European Parliament, the Council of the European Union and the European Commission. The EU General Data Protection Regulation which, it is anticipated, will be officially adopted in mid-2016, will introduce new data protection requirements in the EU, as well as substantial fines for breaches of the data protection rules. The EU General Data Protection Regulation, which will be applicable two years after the date of its publication in the Official Journal for the European Union, will increase our responsibility and liability in relation to personal

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data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules.

Our relationships with customers and third-party payors are subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians, distributors and third-party payors play a primary role in the distribution, recommendation and prescription of any pharmaceutical product for which we obtain marketing approval. Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements through which we market, sell and distribute any products for which we have obtained or may obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

The federal healthcare Anti-Kickback Statute prohibits any person from, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, leasing, ordering or arranging for or recommending of any good or service for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute is subject to evolving interpretation and has been applied by government enforcement officials to a number of common business arrangements in the pharmaceutical industry. The government can establish a violation of the Anti-Kickback Statute without proving that a person or entity had actual knowledge of the statute or specific intent to violate it. There are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution; however, those exceptions and safe harbors are drawn narrowly. Failure to meet all of the requirements of a particular statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute, but the legality of the arrangement will be evaluated on a case-by-case basis based on the totality of the facts and circumstances. We seek to comply with the available statutory exemptions and safe harbors whenever possible, but our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants or patient assistance programs.

The federal civil False Claims Act imposes civil penalties, and provides for whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment of government funds that are false or fraudulent, or knowingly making, or using or causing to be made or used, a false record or statement material to a false or fraudulent claim to avoid, decrease, or conceal an obligation to pay money to the federal government. In recent years, several pharmaceutical and other healthcare companies have faced enforcement actions under the federal False Claims Act for, among other things, allegedly submitting false or misleading pricing information to government health care programs and providing free product to customers with the expectation that the customers would bill federal programs for the product. Federal enforcement agencies also have showed increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement and co-pay support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. Other companies have faced enforcement actions for causing false claims to be submitted because of the company's marketing the product for unapproved, and thus non-reimbursable, uses. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute

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constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. False Claims Act liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties of \$5,500 to \$11,000 per false claim or statement. Because of the potential for large monetary exposure, healthcare and pharmaceutical companies often resolve allegations without admissions of liability for significant and material amounts to avoid the uncertainty of treble damages and per claim penalties that may be awarded in litigation proceedings. Companies may be required, however, to enter into corporate integrity agreements with the government, which may impose substantial costs on companies to ensure compliance. Criminal prosecution is also possible for making or presenting a false or fictitious or fraudulent claim to the federal government.

HIPAA, among other things, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HIPAA also prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services.

The federal Physician Payment Sunshine Act, being implemented as the Open Payments Program, imposes annual reporting requirements on certain manufacturers of drugs, devices, or biologics for payments and other transfers of value by them, directly or indirectly, to physicians (including physician family members) and teaching hospitals, as well as ownership and investment interests held by physicians. A manufacturer's failure to submit timely, accurately and completely the required information for all payments, transfers of value or ownership or investment interests may result in civil monetary penalties of up to an aggregate of \$150,000 per year, and up to an aggregate of \$1 million per year for "knowing failures." Manufacturers must submit reports by the 90th day of each calendar year.

Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. Several states also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products in those states and to report gifts and payments to individual health care providers in those states. Some of these states also prohibit certain marketing-related activities, including the provision of gifts, meals, or other items to certain health care providers. In addition, several states require pharmaceutical companies to implement compliance programs or marketing codes.

Similar restrictions imposed on the promotion and marketing of medicinal products in the EU and other countries, including restrictions prohibiting the promotion of a compound prior to its approval. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we may decide not to directly promote or market our products, inappropriate activity by our any international distribution partners could have implications for us.

The shifting commercial compliance environment and the need to build and maintain robust and expandable systems to comply with different compliance or reporting requirements in multiple jurisdictions increase the possibility that we or our partners may fail to comply fully with one or more of these requirements. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with applicable fraud

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and abuse or other healthcare laws and regulations or guidance. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we do or expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our financial condition and divert resources and the attention of our management from operating our business.

Our business and operations, including the use of hazardous and biological materials may result in liabilities with respect to environmental, health and safety matters.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical, biological and radioactive materials. In addition, our operations produce hazardous waste products, including hazardous waste. Federal, state and local laws and regulations govern the use, manufacture, management, storage, handling and disposal of hazardous materials and wastes. We may incur significant additional costs or liabilities to comply with, or for violations of, these and other applicable laws in the future. Also, even if we are in compliance with applicable laws, we cannot completely eliminate the risk of contamination or injury resulting from hazardous materials and we may incur liability as a result of any such contamination or injury. Further, in the event of a release of or exposure to hazardous materials, including at the sites we currently or formerly operate or at sites such as landfills where we send wastes for disposal, we could be held liable for cleanup costs or damages or subject to other costs or penalties and such liability could exceed our resources. We do not have any insurance for liabilities arising from hazardous materials or under environmental laws. Compliance with or liability under applicable environmental laws and regulations or with respect to hazardous materials may be expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, which could cause the price of our securities to fall.

RISKS RELATING TO OUR ORDINARY SHARES

The market price for our shares has and may continue to fluctuate widely, and may result in substantial losses for purchasers of our ordinary shares.

Our ordinary shares began trading on June 3, 2014, and the market price for our shares has and may continue to fluctuate widely, and may result in substantial losses for purchasers of our ordinary shares. To date, there is limited securities analyst coverage of our company. Limited securities analyst coverage of our company and shares is likely to reduce demand for our shares from potential investors, which likely will reduce the market price for our shares. To the extent that historically low trading volumes for our ordinary shares continues, our stock price may fluctuate significantly more than the stock market as a whole or the stock prices of similar companies. Without a larger public float of actively traded shares, our ordinary shares are likely to be more sensitive to changes in sales volumes, market fluctuations and events or perceived events with respect to our business, than the shares of common stock of companies with broader public ownership, and as a result, the trading prices for our ordinary shares may be more volatile. Among other things, trading of a relatively small volume of ordinary shares may have a greater effect on the trading price than would be the case if our public float of actively traded shares were larger.

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Market prices for securities of biotechnology and biopharmaceutical companies have been highly volatile, and we expect such volatility to continue for the foreseeable future, so that investment in our ordinary shares involves substantial risk. By separating from Innoviva, there is a risk that our company may be more susceptible to market fluctuations and other adverse events than we would have been were we still a part of Innoviva. Additionally, the stock market from time to time has experienced significant price and volume fluctuations unrelated to the operating performance of particular companies.

The following are some of the factors that may have a significant effect on the market price of our ordinary shares:

any adverse developments or results or perceived adverse developments or results with respect to the GSK-Partnered Respiratory Programs, including, without limitation, any delays in development in these programs, any halting of development in these programs, any difficulties or delays encountered with regard to the FDA or other regulatory authorities in these programs, or any indication from clinical or non-clinical studies that the compounds in such programs are not safe or efficacious;

any further adverse developments or perceived adverse developments with respect to the commercialization of VIBATIV, including whether Pfizer's acquisition of Hospira in 2015 will lead to changes in Hospira's operations which may adversely impact our single source of supply for VIBATIV drug product;

whether we achieve increased sales for VIBATIV;

any announcements of developments with, or comments by, the FDA or other regulatory authorities with respect to products we or our partners have under development or have commercialized;

any adverse developments or agreements or perceived adverse developments or agreements with respect to the relationship of Innoviva or TRC, on the one hand, and GSK, on the other hand, including any such developments or agreements resulting from or relating to the Spin-Off;

any adverse developments or perceived adverse developments with respect to our relationship with any of our research, development or commercialization partners, including, without limitation, disagreements that may arise between us and any of those partners, including any such developments resulting from or relating to the Spin-Off;

any adverse developments or perceived adverse developments in our programs with respect to partnering efforts or otherwise;

announcements of patent issuances or denials, technological innovations or new commercial products by us or our competitors;

publicity regarding actual or potential study results or the outcome of regulatory review relating to products under development by us, our partners or our competitors;

regulatory developments in the United States and foreign countries;

announcements with respect to governmental or private insurer reimbursement policies;

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announcements of equity or debt financings;

economic and other external factors beyond our control;

loss of key personnel;

likelihood of our ordinary shares to be more sensitive to changes in sales volume, market fluctuations and events or perceived events with respect to our business due to our small public float;

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low public market trading volumes for our ordinary shares related in part to the concentration of ownership of our shares;

developments or disputes as to patent or other proprietary rights;

approval or introduction of competing products and technologies;

results of clinical trials;

failures or unexpected delays in timelines for our potential products in development, including the obtaining of regulatory approvals;

delays in manufacturing adversely affecting clinical or commercial operations;

fluctuations in our operating results;

market reaction to announcements by other biotechnology or pharmaceutical companies;

initiation, termination or modification of agreements with our collaborators or disputes or disagreements with collaborators;

litigation or the threat of litigation;

public concern as to the safety of drugs developed by us; and

comments and expectations of results made by securities analysts or investors.

If any of these factors causes us to fail to meet the expectations of securities analysts or investors, or if adverse conditions prevail or are perceived to prevail with respect to our business, the price of the ordinary shares would likely drop significantly. A significant drop in the price of a company's securities often leads to the filing of securities class action litigation against the company. This type of litigation against us could result in substantial costs and a diversion of management's attention and resources.

Concentration of ownership will limit your ability to influence corporate matters.

Based on our review of publicly available filings, as of March 31, 2016 GSK beneficially owned approximately 23.3% of our outstanding ordinary shares and our directors, executive officers and investors affiliated with these individuals beneficially owned approximately 7.4% of our outstanding ordinary shares. Based on our review of publicly available filings, as of March 31, 2016 our three largest shareholders other than GSK collectively owned approximately 33.5% of our outstanding ordinary shares. GSK also has a right to maintain its percentage ownership in our company under the Governance Agreement, including by participating in offerings of our ordinary shares such as this offering, although GSK has waived its right to participate in this offering. These shareholders and GSK could control the outcome of actions taken by us that require shareholder approval, including a transaction in which shareholders might receive a premium over the prevailing market price for their shares.

Certain provisions in our constitutional documents may discourage our acquisition by a third party, which could limit your opportunity to sell shares at a premium.

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Our constitutional documents include provisions that could limit the ability of others to acquire control of us, modify our structure or cause us to engage in change-of-control transactions, including, among other things, provisions that:

require supermajority shareholder voting to effect certain amendments to our amended and restated memorandum and articles of association;

establish a classified board of directors;

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restrict our shareholders from calling meetings or acting by written consent in lieu of a meeting;

limit the ability of our shareholders to propose actions at duly convened meetings; and

authorize our board of directors, without action by our shareholders, to issue preferred shares and additional ordinary shares.

These provisions could have the effect of depriving you of an opportunity to sell your ordinary shares at a premium over prevailing market prices by discouraging third parties from seeking to acquire control of us in a tender offer or similar transaction.

Our shareholders may face difficulties in protecting their interests because we are incorporated under Cayman Islands law.

Our corporate affairs are governed by our amended and restated memorandum and articles of association, by the Companies Law (2013 Revision) (as amended) of the Cayman Islands and by the common law of the Cayman Islands. The rights of our shareholders and the fiduciary responsibilities of our directors under the laws of the Cayman Islands are different from those under statutes or judicial precedent in existence in jurisdictions in the U.S. Therefore, you may have more difficulty in protecting your interests than would shareholders of a corporation incorporated in a jurisdiction in the U.S., due to the different nature of Cayman Islands law in this area.

Shareholders of Cayman Islands exempted companies such as our company have no general rights under Cayman Islands law to inspect corporate records and accounts or to obtain copies of lists of shareholders. Our directors have discretion under our amended and restated memorandum and articles of association to determine whether or not, and under what conditions, our corporate records may be inspected by our shareholders, but are not obliged to make them available to our shareholders. This may make it more difficult for you to obtain the information needed to establish any facts necessary for a shareholder motion or to solicit proxies from other shareholders in connection with a proxy contest.

Our Cayman Islands counsel, Maples and Calder, is not aware of any reported class action having been brought in a Cayman Islands court. Derivative actions have been brought in the Cayman Islands courts, and the Cayman Islands courts have confirmed the availability for such actions. In most cases, the company will be the proper plaintiff in any claim based on a breach of duty owed to it, and a claim against (for example) the company's officers or directors usually may not be brought by a shareholder. However, based on English authorities, which would in all likelihood be of persuasive authority and be applied by a court in the Cayman Islands, exceptions to the foregoing principle apply in circumstances in which:

a company is acting, or proposing to act, illegally or beyond the scope of its authority;

the act complained of, although not beyond the scope of the authority, could be effected if duly authorized by more than the number of votes which have actually been obtained; or

those who control the company are perpetrating a "fraud on the minority."

A shareholder may have a direct right of action against the company where the individual rights of that shareholder have been infringed or are about to be infringed.

There is uncertainty as to shareholders' ability to enforce certain foreign civil liabilities in the Cayman Islands.

We are incorporated as an exempted company limited by shares with limited liability under the laws of the Cayman Islands. A material portion of our assets are located outside of the United States. As a result, it may be difficult for our shareholders to enforce judgments against us or judgments

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obtained in U.S. courts predicated upon the civil liability provisions of the federal securities laws of the United States or any state of the United States.

We have been advised by our Cayman Islands legal counsel, Maples and Calder, that the courts of the Cayman Islands are unlikely (i) to recognize or enforce against Theravance Biopharma judgments of courts of the United States predicated upon the civil liability provisions of the securities laws of the United States or any State; and (ii) in original actions brought in the Cayman Islands, to impose liabilities against Theravance Biopharma predicated upon the civil liability provisions of the securities laws of the United States or any State, on the grounds that such provisions are penal in nature. However, in the case of laws that are not penal in nature, although there is no statutory enforcement in the Cayman Islands of judgments obtained in the United States, the courts of the Cayman Islands will recognize and enforce a foreign money judgment of a foreign court of competent jurisdiction without retrial on the merits based on the principle that a judgment of a competent foreign court imposes upon the judgment debtor an obligation to pay the sum for which judgment has been given provided certain conditions are met. For a foreign judgment to be enforced in the Cayman Islands, such judgment must be final and conclusive and for a liquidated sum, and must not be in respect of taxes or a fine or penalty, inconsistent with a Cayman Islands' judgment in respect of the same matter, impeachable on the grounds of fraud or obtained in a manner, and or be of a kind the enforcement of which is, contrary to natural justice or the public policy of the Cayman Islands (awards of punitive or multiple damages may well be held to be contrary to public policy). A Cayman Islands' court, including The Grand Court of the Cayman Islands, may stay proceedings if concurrent proceedings are being brought elsewhere, which would delay proceedings and make it more difficult for our shareholders to bring action against us.

ADDITIONAL RISKS RELATING TO THIS OFFERING

Our management team may invest or spend the net proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of the net proceeds from this offering. We intend to use the net proceeds from the sale of ordinary shares offered by this prospectus supplement for general corporate purposes, which may include, among other things, research activities, preclinical and clinical development of existing product candidates, manufacture of pre-clinical, clinical and commercial drug supplies, selling and marketing expenses, capital expenditures, working capital, general and administrative expenses and acquisitions of technology or drug candidates. We do not currently have any commitments with regard to any such acquisitions or other strategic transactions. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our ordinary shares.

You may experience future dilution as a result of future equity or equity-linked offerings.

In order to raise additional capital, we may in the future offer additional ordinary shares or other securities convertible into or exchangeable for our ordinary shares. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater 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 shareholders. The price per share at which we sell additional ordinary shares or other securities convertible into or exchangeable for our ordinary shares in future transactions may be higher or lower than the price per share in this offering.

Table of Contents**USE OF PROCEEDS**

We estimate that our net proceeds from the sale of the ordinary shares that we are offering will be approximately \$93.6 million, or approximately \$107.7 million if the underwriters exercise in full their option to purchase additional shares, based on the public offering price of \$21.00 per share, after deducting the underwriting discount and estimated offering expenses payable by us.

We intend to use the net proceeds from the sale of ordinary shares offered by this prospectus supplement for general corporate purposes, which may include, among other things, research activities, preclinical and clinical development of product candidates, manufacture of pre-clinical, clinical and commercial drug supplies, selling and marketing expenses, capital expenditures, working capital, general and administrative expenses and acquisitions of technology or drug candidates. We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures, and we do not currently have any commitments with regard to any such acquisitions or other strategic transactions. As a result, our management will have broad discretion to allocate the net proceeds of this offering. Pending the application of the net proceeds for these purposes, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities.

PRICE RANGE OF OUR ORDINARY SHARES

Our ordinary shares are listed on The NASDAQ Global Market under the symbol "TBPH." The following table summarizes the high and low closing sales prices for our ordinary shares as reported by The NASDAQ Global Market for the period indicated:

| | High | Low |
|-----------------------------------|----------|----------|
| 2016 | | |
| First Quarter | \$ 18.80 | \$ 13.35 |
| Second Quarter (through April 28) | 24.20 | 19.69 |
| 2015 | | |
| First Quarter | \$ 21.73 | \$ 14.70 |
| Second Quarter | 18.63 | 12.57 |
| Third Quarter | 14.80 | 10.88 |
| Fourth Quarter | 19.51 | 11.13 |
| 2014 | | |
| Second Quarter (beginning June 2) | \$ 34.87 | \$ 19.50 |
| Third Quarter | 33.99 | 23.05 |
| Fourth Quarter | 23.19 | 13.33 |

The last reported sale price for our ordinary shares on The NASDAQ Global Market on April 28, 2016 was \$21.16. As of April 26, 2016, we had approximately 111 shareholders of record.

DIVIDEND POLICY

We have never declared or paid cash dividends and do not intend to declare or pay cash dividends on our ordinary shares in the foreseeable future.

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CAPITALIZATION

The following table sets forth our cash, cash equivalents and marketable securities and capitalization as of December 31, 2015,

on an actual basis; and

on an as adjusted basis to give effect to the issuance and sale by us of 4,765,000 shares in this offering, and the receipt of the net proceeds from our sale of these shares, at the assumed public offering price of \$21.00 per share, after deducting the underwriting discount and estimated offering expenses payable by us (assuming no exercise of the underwriters' option to purchase additional shares).

You should read this table in conjunction with the sections titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes appearing in our Annual Report on Form 10-K for the year ended December 31, 2015, incorporated by reference in this prospectus supplement.

| | As of December 31, 2015 | |
|--|---|------------------------------------|
| | Actual (in thousands, except per share data) (audited) | As Adjusted (unaudited) |
| Cash, cash equivalents and marketable securities | \$ 215,294 | \$ 308,927 |
| Shareholders' equity | | |
| Preferred shares, \$0.00001 par value: 230 shares authorized, no shares issued or outstanding | | |
| Ordinary shares, \$0.00001 par value: 200,000 shares authorized; 37,981 shares issued and outstanding, actual; 42,746 shares issued and outstanding, as adjusted | | |
| Additional paid-in capital | 564,691 | 658,324 |
| Accumulated other comprehensive loss | (70) | (70) |
| Accumulated deficit | (321,556) | (321,556) |
| Total shareholders' equity | 243,065 | 336,698 |
| Total capitalization | \$ 243,065 | \$ 336,698 |

The number of shares in the table above excludes as of December 31, 2015:

2,311,164 ordinary shares issuable upon the exercise of outstanding options to purchase our ordinary shares having a weighted-average exercise price of \$23.07 per share;

2,147,461 ordinary shares reserved for issuance pursuant to future awards under our 2013 Equity Incentive Award Plan, and any addendums thereto;

266,450 ordinary shares reserved for issuance pursuant to future awards under our 2014 New Employee Equity Incentive Plan;

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929,143 ordinary shares reserved for issuance pursuant to future awards under our 2013 Employee Share Purchase Plan; and

2,988,041 ordinary shares issuable upon vesting of outstanding restricted share units.

In addition, the number of ordinary shares shown above excludes: 1,301,015 ordinary shares sold to GSK on March 17, 2016; 769,996 ordinary shares issued in March and April 2016 under at-the market offerings pursuant to our sales agreement with Cantor; 1,899,056 and 379,811 shares automatically added to our 2013 Equity Incentive Award Plan and 2013 Employee Share Purchase Plan, respectively,

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on January 1, 2016; grants of 107,875 options under our 2014 New Employee Equity Incentive Plan during 2016 having a weighted-average exercise price of \$16.05; and the following grants under the 2013 Equity Incentive Award Plan during 2016: restricted share units issuable for 2,232,373, and 1,575,000 restricted shares.

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**MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR
U.S. HOLDERS OF ORDINARY SHARES**

The following summary discusses material U.S. federal income tax consequences of the ownership and disposition by U.S. Holders of our ordinary shares, as described below. This discussion is based upon the Code, Treasury Regulations, published positions of the IRS, judicial decisions and other applicable authorities, all as currently in effect, and all of which are subject to change or differing interpretations, possibly with retroactive effect. Any such change could affect the accuracy of this discussion.

As discussed above under "Risk Factors *We may be treated as a U.S. corporation for U.S. federal income tax purposes,*" although Theravance Biopharma does not expect to be treated as a U.S. corporation under Section 7874 of the Code, the IRS may disagree without our conclusion on this point or there could be changes to the law that could result in our being treated as a U.S. corporation. If we were treated as a U.S. corporation for U.S. federal income tax purposes, the U.S. tax consequences to holders of ordinary shares would be significantly different. In particular, future cash distributions made by us to holders who are not "U.S. Holders" could be subject to withholding tax at a 30% rate or a reduced rate specified by an applicable income tax treaty. Holders should consult their tax advisers about the U.S. tax consequences of holding ordinary shares if Theravance Biopharma were treated as a U.S. corporation. The remainder of the discussion below assumes that Theravance Biopharma is not treated as a U.S. corporation.

The following discussion is limited to U.S. Holders who hold our ordinary shares as capital assets within the meaning of Section 1221 of the Code. This summary does not discuss all tax considerations that may be relevant to holders of our ordinary shares in light of their particular circumstances, nor does it address the consequences to holders of our ordinary shares subject to special treatment under the U.S. federal income tax laws, such as tax-exempt entities, partnerships (including entities treated as partnerships for U.S. federal income tax purposes), persons who acquire our ordinary shares pursuant to the exercise of employee stock options or otherwise as compensation, financial institutions, insurance companies, dealers or traders in securities, and persons who hold our ordinary shares as part of a straddle, hedge, conversion, constructive sale, synthetic security, integrated investment or other risk-reduction transaction for U.S. federal income tax purposes. This discussion does not address any U.S. federal estate, gift or other non-income tax consequences or any state, local or foreign tax consequences, or the consequences of the alternative minimum tax or the Medicare tax on net investment income.

Prospective purchasers of our ordinary shares should consult their tax advisors as to the particular tax consequences to them of the ownership and disposition of our ordinary shares.

For purposes of this discussion, a U.S. Holder is a beneficial owner of our ordinary shares that is, for U.S. federal income tax purposes:

an individual who is a citizen or a resident of the United States;

a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized under the laws of the United States or any state or political subdivision thereof;

an estate, the income of which is subject to United States federal income taxation regardless of its source; or

a trust, if (i) a court within the United States is able to exercise primary jurisdiction over its administration and one or more U.S. persons have the authority to control all of its substantial decisions, or (ii) in the case of a trust that was treated as a domestic trust under the law in effect before 1997, a valid election is in place under applicable Treasury Regulations.

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If a partnership (including any entity treated as a partnership for U.S. federal income tax purposes) holds our ordinary shares, the tax treatment of a partner in the partnership generally will depend upon the status of the partner and the activities of the partnership. A partner of a partnership holding our ordinary shares should consult its tax advisor as to the particular U.S. federal income tax consequences applicable to them.

Owning or Disposing of our Ordinary Shares

Subject to the PFIC rules discussed below, distributions with respect to our ordinary shares (which for these purposes will include the amount of any non-U.S. taxes withheld therefrom) should generally be includible in the gross income of a U.S. Holder on the date of receipt as foreign source dividend income to the extent that such distributions are paid out of our current or accumulated earnings and profits as determined under U.S. federal income tax principles. Such distributions will not be eligible for the dividends-received deduction generally allowed to U.S. corporations.

Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be eligible for taxation as "qualified dividend income" and therefore may be taxable at rates applicable to long-term capital gains. U.S. Holders should consult their tax advisers regarding the availability of these favorable rates on dividends in their particular circumstances.

To the extent we pay dividends in a currency other than the U.S. dollar, the amount of any dividend paid to U.S. Holders in such currency will (subject to the PFIC rules discussed below) be includible in income in a U.S. dollar amount calculated by reference to the exchange rate in effect on the date of receipt, regardless of whether the amount of such dividend is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency exchange gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency exchange gain or loss if the dividend is converted into U.S. dollars after the date of receipt. In general, foreign currency exchange gain or loss will be treated as U.S.-source ordinary gain or loss for foreign tax credit purposes.

Subject to certain limitations, including the PFIC rules discussed below, non-U.S. taxes (if any) withheld from or paid on dividend distributions generally will be eligible for credit against the U.S. Holder's U.S. federal income taxes. The limitation on foreign taxes eligible for credit is calculated separately with respect to specific classes of income. The foreign tax credit rules are complex, and U.S. Holders are urged to consult their tax advisors regarding the availability of foreign tax credits in their particular circumstances.

Subject to the PFIC rules discussed below, a U.S. Holder will generally recognize a capital gain or loss for U.S. federal income tax purposes on the sale or disposition of our ordinary shares equal to the difference between the amount realized on the sale or disposition and such U.S. Holder's tax basis in the ordinary shares and such capital gain or loss will be long-term capital gain or loss if the U.S. Holder's holding period for such ordinary shares exceeds one year as of the date of sale or disposition. Any gain or loss generally will be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

Passive Foreign Investment Company Status

We do not expect to be a "passive foreign investment company" (a "PFIC") for U.S. federal income tax purposes for our current taxable year or in the foreseeable future. In general, a non-U.S. corporation is a PFIC for any taxable year in which (i) 75% or more of its gross income consists of passive income or (ii) 50% or more of the average quarterly value of its assets consists of assets that produce, or are held for the production of, passive income. For purposes of the above calculations, a non-U.S. corporation that owns directly or indirectly at least 25% by value of the shares of another

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corporation is treated as if it held its proportionate share of the assets of the other corporation and received directly its proportionate share of the income of the other corporation. Passive income generally includes dividends, interest, royalties and rents and certain gains. Because a company's PFIC status depends on the composition of a company's income and assets and the market value of its assets from time to time, there can be no assurance that we will not be a PFIC for any taxable year. The treatment of U.S. Holders of our ordinary shares in some cases will be materially different from that described above if, at any relevant time, Theravance Biopharma is a PFIC. If we are a PFIC for any taxable year during which a U.S. Holder holds our ordinary shares, unless the U.S. Holder makes a mark-to-market election or QEF election (each as described below) with respect to the ordinary shares, the U.S. Holder generally will, except as discussed below, be subject to special tax rules that have a penalizing effect, regardless of whether we remain a PFIC for future taxable years, on (i) any excess distribution that we make to the U.S. Holder (which generally means any distribution paid during a taxable year to a U.S. Holder that is greater than 125% of the average annual distributions paid in the three preceding taxable years or, if shorter, the U.S. Holder's holding period for the ordinary shares), and (ii) any gain realized on the sale or other disposition, including, under certain circumstances, a pledge, of ordinary shares. Under the PFIC rules:

the excess distribution and/or gain will be allocated ratably over the U.S. Holder's holding period for the ordinary shares;

the amount allocated to the current taxable year and any taxable years in the U.S. Holder's holding period prior to the first taxable year in which we are a PFIC (each, a pre-PFIC year) will be taxable as ordinary income;

the amount allocated to each prior taxable year, other than the current taxable year or a pre-PFIC year, will be subject to tax at the highest tax rate in effect applicable to the individuals or corporations, as appropriate, for that year; and

will be increased by an additional tax equal to interest on the resulting tax deemed deferred with respect to each prior taxable year, other than a pre-PFIC year.

If we are a PFIC for any taxable year during which a U.S. Holder holds our ordinary shares and any of our non-United States subsidiaries is also a PFIC, such U.S. Holder would be treated as owning a proportionate amount (by value) of the shares of the lower-tier PFIC for purposes of the application of these rules. Each U.S. Holder is advised to consult its tax advisors regarding the application of the PFIC rules to any of our subsidiaries.

Even though we do not currently believe that we are a PFIC, we were a PFIC in 2014. Any U.S. Holders who currently owns any of our ordinary shares that it held while we were or may have been a PFIC should consult its tax advisor.

As an alternative to the foregoing rules, a U.S. Holder of "marketable stock" in a PFIC may make a mark-to-market election with respect to our ordinary shares, provided that such ordinary shares are regularly traded. Our ordinary shares would be treated as "regularly traded" for any calendar year in which more than a de minimis quantity of the ordinary shares were traded on a qualified exchange on at least 15 days during each calendar quarter. The NASDAQ Global Market, where our ordinary shares are listed, is a qualified exchange for this purpose. If a mark-to-market election is made, the U.S. Holder will generally (i) include as ordinary income for each taxable year that we are a PFIC the excess, if any, of the fair market value of ordinary shares held at the end of the taxable year over the adjusted tax basis of such ordinary shares and (ii) deduct as an ordinary loss the excess, if any, of the adjusted tax basis of the ordinary shares over the fair market value of such ordinary shares held at the end of the taxable year, but only to the extent of the net amount previously included in income as a result of the mark-to-market election. The U.S. Holder's adjusted tax basis in the ordinary shares would be adjusted to reflect any income or loss resulting from the mark-to-market election. If a U.S. Holder

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makes an effective mark-to-market election, in each year that we are a PFIC, any gain recognized upon the sale or other disposition of the ordinary shares will be treated as ordinary income and loss will be treated as ordinary loss, but only to the extent of the net amount previously included in income as a result of the mark-to-market election.

If a U.S. Holder makes a mark-to-market election in respect of a corporation classified as a PFIC and such corporation ceases to be classified as a PFIC, the U.S. Holder will not be required to take into account the mark-to-market gain or loss described above during any period that such corporation is not classified as a PFIC.

Because a mark-to-market election cannot be made for any lower-tier PFICs that we may own, a U.S. Holder who makes a mark-to-market election with respect to our ordinary shares may continue to be subject to the general PFIC rules with respect to such U.S. Holder's indirect interest in any of our non-United States subsidiaries that is classified as a PFIC.

A U.S. Holder of ordinary shares in a PFIC may instead make a qualified electing fund election ("QEF election"), with respect to such ordinary shares. A U.S. Holder who makes a timely QEF election with respect to our ordinary shares must report for U.S. federal income tax purposes their pro rata share of our ordinary earnings and net capital gain, if any, for each taxable year for which we are a PFIC that ends with or within such U.S. Holder's taxable year, regardless of whether or not they receive any distributions on the ordinary shares that they own. No portion of any such inclusions of ordinary earnings would be eligible to be treated as "qualified dividend income." For a non-corporate U.S. Holder, any such net capital gain inclusions would be eligible for taxation at the preferential capital gains tax rates. For ordinary shares held by a regulated investment company, such ordinary earnings and net capital gain inclusions will be treated as qualifying income described in Section 851(b)(2)(A) of the Code. A U.S. Holder's adjusted tax basis in our ordinary shares would be increased to reflect any taxed but undistributed earnings and profits. Any distribution of earnings and profits that had been previously taxed would not be taxed again when a U.S. Holder receives such distribution, but would result in a corresponding reduction in the adjusted tax basis in our ordinary shares. A U.S. Holder would not, however, be entitled to a deduction for their pro rata share of any losses a PFIC incurs with respect to any year. A U.S. Holder generally would recognize capital gain or loss on the sale, exchange or other disposition of our ordinary shares. A U.S. Holder may make a timely QEF election with respect to our ordinary shares by filing IRS Form 8621 with their U.S. federal income tax return for the first year in which we are a PFIC and such U.S. Holder holds our ordinary shares. If we are a PFIC for any taxable year, we will make available to U.S. Holders the necessary information in order to make a QEF election as described above.

Dividends that we pay on our ordinary shares will not be eligible for the reduced tax rate that applies to qualified dividend income if we are classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year. In addition, if a U.S. Holder owns our ordinary shares during any taxable year that we are a PFIC, such U.S. Holder must file an annual report with the IRS, subject to certain limited exceptions. Each U.S. Holder is urged to consult its tax advisor concerning the United States federal income tax consequences of owning and disposing of our ordinary shares if we are or become a PFIC, including the possibility of making a mark-to-market election or a qualified electing fund election.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries may be subject to information reporting and to backup withholding, unless (i) the U.S. Holder is a corporation or other "exempt recipient" and or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding. The amount of any backup withholding from a

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payment to a U.S. Holder will be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

Certain U.S. Holders are required to report information relating to an interest in our ordinary shares, subject to exceptions (including an exception for ordinary shares held in accounts maintained by certain financial institutions), by attaching a completed IRS Form 8938, Statement of Specified Foreign Financial Assets, with their tax return for each year in which they hold an interest in our ordinary shares. U.S. Holders are urged to consult their own tax advisors regarding information reporting requirements relating to their ownership of our ordinary shares.

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**CERTAIN IRISH TAX CONSIDERATIONS FOR HOLDERS OF
ORDINARY SHARES**

We became an Irish tax resident effective July 1, 2015, though we remain incorporated in the Cayman Islands. The following is a discussion of certain Irish tax considerations with respect to the ownership and disposition of our ordinary shares applicable to investors who acquire such shares in this offering.

THIS SUMMARY IS FOR GENERAL INFORMATION ONLY AND IS NOT INTENDED TO CONSTITUTE A COMPLETE DESCRIPTION OF ALL TAX CONSEQUENCES RELATING TO THE OWNERSHIP AND DISPOSITION OF OUR ORDINARY SHARES. PROSPECTIVE HOLDERS OF OUR ORDINARY SHARES SHOULD REFER TO DISCLOSURES WITH RESPECT TO OTHER TAX MATTERS IN DOCUMENTS INCORPORATED BY REFERENCE INTO THIS PROSPECTUS SUPPLEMENT AND CONSULT WITH THEIR TAX ADVISORS REGARDING THE TAX CONSEQUENCES TO THEM (INCLUDING THE APPLICATION AND EFFECT OF ANY STATE, LOCAL, FOREIGN INCOME AND OTHER TAX LAWS) OF THE OWNERSHIP AND DISPOSITION OF OUR ORDINARY SHARES UNDER THE LAWS OF THEIR COUNTRY OF RESIDENCE, CITIZENSHIP OR DOMICILE.

THE FOLLOWING CONSIDERATIONS ARE BASED ON THE LAWS AND PRACTICE OF THE IRISH REVENUE COMMISSIONERS CURRENTLY IN FORCE IN IRELAND AND MAY BE SUBJECT TO CHANGE. IT DEALS WITH HOLDERS WHO BENEFICIALLY OWN OUR ORDINARY SHARES AS AN INVESTMENT. PARTICULAR RULES NOT DISCUSSED BELOW MAY APPLY TO CERTAIN CLASSES OF TAXPAYERS HOLDING OUR ORDINARY SHARES, SUCH AS DEALERS IN SECURITIES, TRUSTS, ETC. THE SUMMARY DOES NOT CONSTITUTE LEGAL OR TAX ADVICE.

Irish Stamp Duty

No Irish stamp duty will be payable in respect of any shares forming part of this offering. No Irish stamp duty will be payable in respect of a sale of our ordinary shares after this offering unless such sale relates to shares in an Irish incorporated company or Irish land or mineral rights. Currently the Company is incorporated in the Cayman Islands and is only an Irish tax resident.

Irish Tax on Capital Gains on a disposal of our ordinary shares

A liability to Irish tax on capital gains on a disposal of our ordinary shares depends on the individual circumstances of each shareholder.

Non-Irish resident / ordinarily resident shareholders. Shareholders should not be subject to Irish tax on capital gains on a disposal of our ordinary shares if such holders are neither resident nor ordinarily resident in Ireland and do not hold such shares in connection with a trade carried on by such holder in Ireland through a branch or agency.

Irish resident shareholders. Shareholders who are resident or ordinarily resident in Ireland for tax purposes, or corporate shareholders who hold their shares in connection with a trade carried on by such holder in Ireland through a branch or agency may be subject to Irish tax on capital gains at the rate of 33% if they dispose of our ordinary shares. Shareholders falling into this category should consult their own tax advisers as to the tax consequences of such a disposal.

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Dividends

We do not currently intend to pay dividends to our shareholders. A payment of a dividend by an Irish resident entity is subject to dividend withholding tax at the current rate of 20%, however a number of exemptions apply including exemptions for dividends paid to:

an individual shareholder (not being a company) who is neither resident nor ordinarily resident in Ireland and who is resident for tax purposes in a Relevant Territory (as described below);

a corporate shareholder which is not resident for tax purposes in Ireland and which is resident for tax purposes in a Relevant Territory provided that the corporate shareholder is not under the control, whether directly or indirectly, of a person or persons who is or are resident in Ireland;

a corporate shareholder which is not resident for tax purposes in Ireland and which is ultimately controlled, directly or indirectly, by persons resident in a Relevant Territory;

a corporate shareholder which is not resident for tax purposes in Ireland and whose principal class of shares (or those of its 75% parent) is substantially and regularly traded on a recognised stock exchange either in a Relevant Territory, Ireland or on such other stock exchange approved by the Minister for Finance; or

a corporate shareholder which is not resident for tax purposes in Ireland and is wholly owned, directly or indirectly, by two or more companies where the principal class of shares of each of such companies is substantially and regularly traded on a recognised stock exchange in a Relevant Territory, Ireland or on such other stock exchange approved by the Minister for Finance.

In this context, Relevant Territory means (i) a Member State of the European Union (other than Ireland) or (ii) a country with which Ireland has a tax treaty in force by virtue of section 826(1) of the Taxes Consolidation Act 1997 ("TCA") or (iii) a country with which Ireland has a tax treaty that is signed and which will come into force once all the ratification procedures set out in section 826(1) TCA have been completed.

Capital Acquisitions Tax

A gift or inheritance comprising of our ordinary shares will be within the charge to capital acquisitions tax (which, subject to available exemptions and reliefs, is currently levied at 33%) if either (i) the disponer or the donee/successor in relation to the gift or inheritance is resident or ordinarily resident in Ireland (or, in certain circumstances, if the disponer is domiciled in Ireland irrespective of his residence or that of the donee/successor) on the relevant date or (ii) if our ordinary shares are regarded as property situate in Ireland (e.g. if the share register is located in Ireland).

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MATERIAL CAYMAN ISLANDS TAX CONSIDERATIONS

The Government of the Cayman Islands will not, under existing legislation, impose any income, corporate or capital gains tax, estate duty, inheritance tax, gift tax or withholding tax upon us or our shareholders. The Cayman Islands is not party to a double tax treaty with any country that is applicable to any payments made to or by us.

We have received on May 20, 2014 an undertaking from the Governor-in-Cabinet of the Cayman Islands that, in accordance with section 6 of the Tax Concessions Law (2011 Revision) of the Cayman Islands, for a period of 20 years from the date of the undertaking, no law which is enacted in the Cayman Islands imposing any tax to be levied on profits, income, gains or appreciations shall apply to us or our operations and, in addition, that no tax to be levied on profits, income, gains or appreciations or which is in the nature of estate duty or inheritance tax shall be payable (i) on or in respect of the shares, debentures or other obligations of ours or (ii) by way of the withholding in whole or in part of a payment of dividend or other distribution of income or capital by us to our members or a payment of principal or interest or other sums due under a debenture or other obligation of ours.

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Table of Contents**UNDERWRITERS**

Leerink Partners LLC and Evercore Group L.L.C. are acting as representatives of each of the underwriters named below and as joint bookrunning managers for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of ordinary shares set forth opposite its name below.

| Underwriter | Number of Ordinary Shares |
|------------------------------------|----------------------------------|
| Leerink Partners LLC | 1,858,350 |
| Evercore Group L.L.C. | 1,620,100 |
| Guggenheim Securities, LLC | 714,750 |
| Robert W. Baird & Co. Incorporated | 571,800 |
| Total | 4,765,000 |

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the ordinary shares sold under the underwriting agreement if any of these shares are purchased. 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 certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the ordinary shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Underwriting Discount

The representatives have advised us that the underwriters propose initially to offer the ordinary shares to the public at the public offering price set forth on the cover of this prospectus supplement and to dealers at that price less a concession not in excess of \$0.7560 per ordinary share. After the initial offering of the ordinary shares, the public offering price, concession or any other term of the offering may be changed by the representatives.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional ordinary shares.

| | Per Ordinary Share | Without Option | Total | With Option |
|----------------------------------|---------------------------|-----------------------|-------------------|--------------------|
| Public offering price | \$ 21.00 | \$ 100,065,000.00 | \$ 115,074,750.00 | |
| Underwriting discount | \$ 1.26 | \$ 6,003,900.00 | \$ 6,904,485.00 | |
| Proceeds, before expenses, to us | \$ 19.74 | \$ 94,061,100.00 | \$ 108,170,265.00 | |

We estimate expenses payable by us in connection with this offering, other than the underwriting discount referred to above, will be approximately \$413,000. We also have agreed to reimburse the

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underwriters for up to \$15,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus supplement, to purchase up to 714,750 additional ordinary shares at the public offering price, less the underwriting discount. The underwriters may only exercise this option to cover sales in excess of the number of ordinary shares listed in the table above. If the underwriters exercise this option, each underwriter will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional ordinary shares proportionate to that underwriter's initial amount reflected in the above table. The underwriters may exercise this option solely for the purpose of covering sales in excess of the aggregate number of ordinary shares listed in the table above.

No Sales of Similar Securities

We and our executive officers and directors have agreed, with certain limited exceptions, that we and they will not, for a period of 90 days after the date of this prospectus supplement, without first obtaining the prior written consent of the representatives, directly or indirectly:

offer, pledge, sell or contract to sell any ordinary shares;

sell any option or contract to purchase any ordinary shares;

purchase any option or contract to sell any ordinary shares;

grant any option, right or warrant for the sale of any ordinary shares;

otherwise dispose of or transfer any ordinary shares;

request or demand that we file a registration statement related to any ordinary shares; or

enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any ordinary shares whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to our ordinary shares and to securities convertible into or exchangeable or exercisable for or repayable with our ordinary shares. It also applies to ordinary shares 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. Notwithstanding the above, this lock-up provision will not apply to us with respect to (1) the issuance of the ordinary shares offered by this prospectus supplement, (2) the issuance and sale of our ordinary shares to GSK pursuant to any exercise by GSK of its right following the end of each calendar quarter to purchase its pro rata portion of ordinary shares that we issued in the preceding quarter (not including the ordinary shares offered by this prospectus supplement, for which GSK has waived its right), (3) our ordinary shares issued pursuant to outstanding options, restricted share units or other rights under our equity incentive plans existing on the date of this prospectus supplement, (4) options, restricted share units or other restricted share awards granted under our equity incentive plans existing on the date of this prospectus supplement, provided that such awards shall not vest or become exercisable prior to the expiration of the lock-up period, (5) our ordinary shares issued upon the exercise of any other option or warrant, settlement of a restricted share unit or the conversion of a security outstanding on the date of this prospectus supplement, or (6) ordinary shares issued pursuant to our employee share purchase plan. In addition, this lock-up provision will not apply to our directors and officers with respect to (1) transfers by bona fide gift, or to any trust for the direct or indirect benefit of the director or officer or an immediate family member, provided that, in each case, the transferee or donee agrees in writing to be

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bound by the lock-up restrictions described above, no filing under the Exchange Act is required or voluntarily made during the lock-up period (other than a Form 5 made after the expiration of the lock-up period) and no public announcement of such transfer is otherwise made, (2) dispositions pursuant to trading plans meeting the requirements of Rule 10b5-1 under the Exchange Act that are in effect as of the date of the lock-up agreement and have been previously disclosed to the representatives, (3) the establishment of a new trading plan meeting the requirements of Rule 10b5-1 under the Exchange Act, provided that such plan does not permit transfers or sales of our ordinary shares during the lock-up period and no public announcement or filing under the Exchange Act regarding the establishment of such plan is required or voluntarily made or (4) the surrender of ordinary shares to us or the sale of ordinary shares upon the vesting or settlement of any restricted share unit or restricted share award held by the director or officer, provided that such surrender or sale is solely for the purpose of covering such director's or officer's tax withholding liability in connection with the vesting or settlement of such award pursuant to a share withholding program or arrangement to provide for sales to cover such tax withholding liability approved by our board of directors or our compensation committee prior to the date of this prospectus supplement.

The NASDAQ Global Market Listing

Our ordinary shares are listed on The NASDAQ Global Market under the symbol "TBPH."

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our ordinary shares. However, the representatives may engage in transactions that stabilize the price of our ordinary shares, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our ordinary shares in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option described above. The underwriters may close out any covered short position by either exercising their option or purchasing ordinary shares in the open market. In determining the source of ordinary shares to close out the covered short position, the underwriters will consider, among other things, the price of ordinary shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing ordinary shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our ordinary shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of ordinary shares made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our ordinary shares or preventing or retarding a decline in the market price of our ordinary shares. As a result, the price of our ordinary shares may be higher than the price that might otherwise exist in the open market. The

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underwriters may conduct these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our ordinary shares. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice. Prior to purchasing the ordinary shares offered hereby, on April 28, 2016, one of the underwriters purchased, on behalf of the syndicate, 29,142 ordinary shares at an average price of \$21.17 per share in stabilizing transactions.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of ordinary shares may be made to the public in that Relevant Member State other than:

- A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or
- C. in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of ordinary shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

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Each person in a Relevant Member State who initially acquires any ordinary shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed 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. In the case of any ordinary shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any ordinary shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

We, the representatives and each of our and the representatives' affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus supplement has been prepared on the basis that any offer of ordinary shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of ordinary shares. Accordingly, any person making or intending to make an offer in that Relevant Member State of ordinary shares which are the subject of the offering contemplated in this prospectus supplement may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the underwriters have authorized, nor do they authorize, the making of any offer of our ordinary shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any ordinary shares 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 shares to be offered so as to enable an investor to decide to purchase or subscribe for the ordinary shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

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LEGAL MATTERS

The validity of the ordinary shares offered hereby will be passed upon for us by Maples and Calder, Cayman Islands. Davis Polk & Wardwell LLP, Menlo Park, California, is counsel to the underwriters in connection with this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated 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 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.

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PROSPECTUS

\$250,000,000

**THERAVANCE BIOPHARMA, INC.
Theravance Biopharma Antibiotics, Inc.
Theravance Biopharma Cayman Holdings, Inc.
Theravance Biopharma Ireland Limited
Theravance Biopharma R&D, Inc.
Theravance Biopharma UK Limited
Theravance Biopharma US, Inc.**

**Debt Securities
Guarantees
Ordinary Shares
Warrants**

We may, from time to time, offer and sell debt securities, ordinary shares and warrants, either separately or in units, in one or more offerings. The debt securities and warrants may be convertible into or exercisable or exchangeable for ordinary shares or debt securities. The aggregate initial offering price of all securities sold under this prospectus will not exceed \$250,000,000.

We will provide specific terms of any offering in a supplement to this prospectus. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby.

We may offer these securities independently or together in any combination for sale directly to investors or through underwriters, dealers or agents. We will set forth the names of any underwriters, dealers or agents and their compensation in the accompanying prospectus supplement or term sheet.

This prospectus may not be used to sell any of these securities unless accompanied by a prospectus supplement.

Our ordinary shares are traded on the Nasdaq Global Market under the symbol "TBPH." On July 8, 2015, the closing price of our ordinary shares on the Nasdaq Global Market was \$11.84 per share.

Investing in our securities involves risks. See the section entitled "Risk Factors" on page 1 of this prospectus and in any accompanying prospectus supplement and in the documents we incorporate by reference in this prospectus.

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Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 16, 2015.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration, or continuous offering, process. Under this shelf registration process, we may, from time to time, issue and sell any combination of debt securities, ordinary shares and warrants, either separately or in units, in one or more offerings with a maximum aggregate offering price of \$250,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering and the offered securities. Any prospectus supplement may also add, update or change information contained in this prospectus. Any statement that we make in this prospectus will be modified or superseded by any inconsistent statement made by us in a prospectus supplement. The registration statement we filed with the SEC includes exhibits that provide more detail of the matters discussed in this prospectus. You should read this prospectus and the related exhibits filed with the SEC and any prospectus supplement, together with additional information described under the heading "Where You Can Find More Information," before making your investment decision.

You should rely only on the information incorporated by reference or provided in this prospectus, any prospectus supplement and the registration statement. We have not authorized anyone else to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We 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 in this prospectus and any prospectus supplement, or incorporated by reference, is accurate only as of the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

Unless the context otherwise requires, references in this prospectus and the accompanying prospectus supplement to "Theravance Biopharma," "we," "us," "our" and other similar pronouns refer to Theravance Biopharma, Inc. and its subsidiaries.

Theravance Biopharma, the Theravance Biopharma logo and VIBATIV are our registered trademarks. Other trademarks, tradenames or service marks of other companies appearing in this prospectus are the property of their respective owners.

RISK FACTORS

Investing in our securities involves risk. The prospectus supplement relating to a particular offering will contain a discussion of risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement and in our Annual Report on Form 10-K, as updated in our Quarterly Reports on Form 10-Q, which are incorporated by reference in this prospectus, together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus. The risks described below and in documents incorporated by reference are not the only ones we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

Our publicly announced net sales target for VIBATIV for 2015 is based on rapid and increasing acceleration of sales growth during the course of the year that may not be achieved and if we revise downward or fail to meet our 2015 net sales targets for VIBATIV, the price of our securities could fall.

Our publicly announced net sales target for VIBATIV for 2015 of approximately \$20 million is based on rapid and increasing acceleration of sales throughout the year, and we currently anticipate that the vast majority of sales will be in the second half of the year. This forecast is based on a number of assumptions, including assumptions about the productivity of new and existing sales representatives, the pace of market penetration, the acceptance of VIBATIV onto formulary by multiple hospitals and

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healthcare systems, the amount of chargebacks and government rebates, and the timing, frequency and impact of price increases, among other factors. Our forecast plans for a significantly higher level of VIBATIV net sales to occur in the fourth quarter versus the third quarter of 2015, so even small delays in market penetration and sales representative productivity, or higher than expected attrition in our sales force, among other factors, could have a material adverse effect on our ability to achieve our targeted 2015 VIBATIV net sales. If we revise our net sales guidance downward in the future or fail to meet our publicly announced 2015 net sales target for VIBATIV or other expectations about our VIBATIV commercialization strategy for these or other reasons, the price of our securities could fall.

THERAVANCE BIOPHARMA, INC.

The mission of Theravance Biopharma is to create value from a unique and diverse set of assets: an approved product; a development pipeline of late-stage assets; and a productive research platform designed for long-term growth.

Our pipeline of internally discovered product candidates includes potential best-in-class opportunities in underserved markets in the acute care setting, representing multiple opportunities for value creation. VIBATIV® (telavancin), our first commercial product, is a once-daily dual-mechanism antibiotic approved in the United States and Europe for certain difficult-to-treat infections. TD-4208 is an investigational long-acting muscarinic antagonist (LAMA) being developed as a potential once-daily, nebulized treatment for chronic obstructive pulmonary disease (COPD). Axelopran (TD-1211) is an investigational potential once-daily, oral treatment for opioid-induced constipation (OIC). Our earlier-stage clinical assets represent novel approaches for potentially treating diseases of the lung and gastrointestinal tract and infectious disease. In addition, we have an economic interest in future payments that may be made by GlaxoSmithKline plc (together with its affiliates, "GSK") pursuant to its agreements with Theravance, Inc. ("Theravance") relating to certain drug development programs, including the combination of fluticasone furoate, umeclidinium, and vilanterol (or the "Closed Triple").

On June 1, 2014, Theravance separated its late-stage respiratory assets partnered with GSK from its biopharmaceutical operations by transferring its discovery, development and commercialization operations (the "Biopharmaceutical Business") and contributing \$393.0 million of cash, cash equivalents and marketable securities into its then wholly-owned subsidiary Theravance Biopharma. On June 2, 2014 Theravance made a pro rata dividend distribution to its stockholders of record on May 15, 2014 of one ordinary share of Theravance Biopharma for every three and one half shares of Theravance common stock outstanding on the record date (the "Spin-Off"). The Spin-Off resulted in Theravance Biopharma operating as an independent, publicly-traded company. Prior to June 2, 2014, Theravance operated the Biopharmaceutical Business.

Corporate Information

Theravance Biopharma was incorporated in the Cayman Islands in July 2013 under the name Theravance Biopharma, Inc. Our registered office address in the Cayman Islands is P.O. Box 309, Uglan House, Grand Cayman, KY1-1104, Cayman Islands and the principal office of our wholly-owned U.S. operating subsidiary Theravance Biopharma US, Inc., is 901 Gateway Boulevard, South San Francisco, California 94080.

Our internet address is www.theravance.com. Information contained on our website does not constitute a part of this prospectus. Our investor relations website is located at <http://investor.theravance.com>. We make available free of charge on our investors relations website under "SEC Filings" our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, our directors' and officers' Section 16 Reports and any amendments to those reports as soon as reasonably practicable after filing such materials with or furnishing such materials to the SEC. The information found on either of our websites is not part of this or any other report that we file with or furnish to the SEC.

FORWARD-LOOKING STATEMENTS

This prospectus contains 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. Such forward-looking statements involve substantial risks, uncertainties and assumptions. All statements in this prospectus, other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans, intentions, expectations and objectives could be forward-looking statements. The words "aim," "anticipates," "believes," "could," "designed," "developed," "drive," "estimates," "expects," "goal," "intends," "may," "mission," "opportunities," "plans," "potential," "projects," "pursuing," "represents," "suggest," "target," "will," "would" and similar expressions (including the negatives thereof) are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions, expectations or objectives disclosed in our forward-looking statements and the assumptions underlying our forward-looking statements may prove incorrect. Therefore, you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and objectives disclosed in the forward-looking statements that we make.

Factors that we believe could cause actual results or events to differ materially from our forward-looking statements include, but are not limited to, those discussed below, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, in the sections "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" and elsewhere in this prospectus. Our forward-looking statements in this prospectus are based on current expectations and we do not assume any obligation to update any forward-looking statements.

USE OF PROCEEDS

Unless we state otherwise in the accompanying prospectus supplement, we intend to use the net proceeds from the sale of securities offered by this prospectus, if any, for general corporate purposes, which may include, among other things, research activities, preclinical and clinical development of existing product candidates, manufacture of pre-clinical, clinical and commercial drug supplies, selling and marketing expenses, capital expenditures, working capital, general and administrative expenses and acquisitions of technology or drug candidates.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges on a historical basis for the periods indicated. The ratios are calculated by dividing earnings by the fixed charges.

| | Three Months Ended | | Year Ended December 31, | | | |
|--|---------------------------|-------------|--------------------------------|-------------|-------------|-------------|
| | March 31, 2015 | 2014 | 2013 | 2012 | 2011 | 2010 |
| Ratio of earnings to fixed charges(1) | | | | | | |

(1) For the purposes of computing ratio of earnings to fixed charges, earnings consist of loss before income taxes plus fixed charges. Fixed charges consist of interest charges and that portion of rental payments under operating leases we believe to be representative of interest. Earnings for the three months ended March 31, 2015 and the years 2014, 2013, 2012, 2011 and 2010 were insufficient to cover fixed charges by \$37.5 million, \$230.7 million, \$156.3 million, \$9.6 million, \$109.3 million and \$79.7 million, respectively.

DESCRIPTION OF DEBT SECURITIES

The following is a summary of the general terms of the debt securities. We will file a prospectus supplement that will contain additional terms when we issue debt securities. The terms presented here, together with the terms in a related prospectus supplement, will be a description of the material terms of the debt securities. You should also read the indenture under which the debt securities are to be issued and the form of debt securities. Such indenture may be supplemented from time to time. We have filed a form of indenture governing different types of debt securities with the SEC as an exhibit to the registration statement of which this prospectus is a part. All capitalized terms have the meanings specified in the indenture.

We may issue, from time to time, debt securities, in one or more series. The debt securities we offer will be issued under an indenture between us, any subsidiary guarantors, and the trustee named in the indenture. These debt securities that we may issue include senior debt securities, guarantees, senior subordinated debt securities, subordinated debt securities, convertible debt securities and exchangeable debt securities. The following is a summary of the material provisions of the form of the indenture filed as an exhibit to the registration statement of which this prospectus is a part. For each series of debt securities, the applicable prospectus supplement for the series will change and supplement the summary below.

General Terms of the Indenture

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. 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. For each series of debt securities, any restrictive covenants for those debt securities will be described in the applicable prospectus supplement relating to such series, including any pricing supplement or term sheet. 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, for United States federal income tax purposes, be treated as if they were issued with "original issue discount," or OID, because of interest payment and other characteristics. Special United States federal income tax considerations applicable to debt securities issued with original issue discount will be described in more detail in any applicable prospectus supplement.

The debt securities may be guaranteed by one or more of Theravance Biopharma Antibiotics, Inc., Theravance Biopharma Cayman Holdings, Inc., Theravance Biopharma Ireland Limited, Theravance Biopharma R&D, Inc., Theravance Biopharma UK Limited, and Theravance Biopharma US, Inc., or other future subsidiaries of Theravance Biopharma, Inc. (the "Subsidiary Guarantors"). Any guarantee by the Subsidiary Guarantors will be a direct obligation of such subsidiary, and such subsidiary may make payments of interest or principal on the debt securities regardless of whether an event of default has occurred with respect to such payments by us. Any guarantee will rank equally with all of the other unsecured and unsubordinated indebtedness of the applicable Subsidiary Guarantor. Terms of any subsidiary guarantees will be more fully described in a prospectus supplement.

You should refer to the prospectus supplement relating to a particular series of debt securities for a description of the following terms of the debt securities offered by that prospectus supplement and by this prospectus:

the title and authorized denominations of those debt securities;

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the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;

the aggregate principal amount of the debt securities and any limit on the aggregate principal amount of that series of debt securities;

the date or dates on which principal and premium, if any, of the debt securities of that series is payable;

the interest rate or rates, and the dates from which interest, if any, on the debt securities of that series will accrue, and the dates when interest is payable or the method by which such dates are to be determined;

the right, if any, to extend the interest payment periods and the duration of the extensions;

whether debt securities are guaranteed by any Subsidiary Guarantors and any deletions from, modifications to, or additions to such guarantees, Events of Default or covenants with respect to such guarantees;

if the amount of payments of principal or interest is to be determined by reference to an index or formula, or based on a coin or currency other than that in which the debt securities are stated to be payable, the manner in which these amounts are determined and the calculation agent, if any, with respect thereto;

the place or places where and the manner in which principal of, premium, if any, and interest, if any, on the debt securities of that series will be payable and the place or places where those debt securities may be presented for transfer and, if applicable, conversion or exchange;

the period or periods within which, the price or prices at which, the currency or currencies in which, and other terms and conditions upon which those debt securities may be redeemed, in whole or in part, at our option or the option of a holder of those securities, if we or a holder is to have that option;

our obligation or right, if any, to redeem, repay or purchase those debt securities pursuant to any sinking fund or analogous provision or at the option of a holder of those securities, and the terms and conditions upon which the debt securities will be redeemed, repaid or purchased, in whole or in part, pursuant to that obligation;

the terms, if any, on which the debt securities of that series will be subordinate in right and priority of payment to our other debt;

the denominations in which those debt securities will be issuable;

if other than the entire principal amount of the debt securities when issued, the portion of the principal amount payable upon acceleration of maturity as a result of a default on our obligations or how this portion will be determined;

whether those debt securities will be issued in fully registered form without coupons or in a form registered as to principal only with coupons or in bearer form with coupons;

whether any securities of that series are to be issued in whole or in part in the form of one or more global securities and the depositary for those global securities;

if other than United States dollars, the currency or currencies in which payment of principal of or any premium or interest on those debt securities will be payable;

if the principal of or any premium or interest on the debt securities of that series is to be payable, or is to be payable at our election or the election of a holder of those securities, in securities or other property, the type and amount of those securities or other property, or the manner of determining that amount, and the period or periods within which, and the terms and conditions upon which, any such election may be made;

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any provisions granting special rights to the holders of debt securities upon the occurrence of specified events;

the events of default and covenants relating to the debt securities that are in addition to, modify or delete those described in this prospectus;

conversion or exchange provisions, if any, including conversion or exchange prices or rates and adjustments thereto;

whether and upon what terms the debt securities may be defeased, if different from the provisions set forth in the indenture;

the nature and terms of any security for any secured debt securities;

the terms applicable to any debt securities issued at a discount from their stated principal amount; and

any other specific terms of any debt securities or guarantees.

The applicable prospectus supplement will present material United States federal income tax considerations for holders of any debt securities and the securities exchange or quotation system on which any debt securities are to be listed or quoted.

Conversion or Exchange Rights

Debt securities may be convertible into or exchangeable for shares of our equity securities or other securities. The terms and conditions of conversion or exchange will be stated in the applicable prospectus supplement. The terms will include, among others, the following:

the conversion or exchange ratio (or the calculation method);

the conversion or exchange period (or how the period will be determined);

provisions regarding our ability or the ability of any holder to convert or exchange the debt securities;

events requiring adjustment to the conversion or exchange ratio; and

provisions affecting conversion or exchange in the event of our redemption of the debt securities.

These terms may also include provisions under which the number or amount of other securities to be received by the holders of the debt securities upon conversion or exchange would be calculated according to the market price of the other securities as of a time stated in the prospectus supplement.

Consolidation, Merger or Sale

We cannot consolidate with or merge with or into, or transfer or lease all or substantially all of our assets to, any person, unless we are the continuing company or unless the successor entity or person to which our assets are transferred or leased is organized under the laws of the Cayman Islands, the British Virgin Islands, Bermuda, Hong Kong, the United States, any state of the United States or the District of Columbia and expressly assumes by a supplemental indenture the due and punctual payment of the principal of, any premium on and any interest on, all the outstanding debt securities and the performance of every covenant and obligation in the indenture to be performed by us. In addition, we cannot complete such a transaction unless immediately after completing the transaction, no event of default under the indenture, and no event that, after notice or lapse of time or both, would become an event of default under the indenture, has occurred and is continuing. When the

successor entity or person to whom our assets are transferred or leased has assumed our obligations under the debt

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securities and the indenture, we will be discharged from all our obligations under the debt securities and the indenture except in limited circumstances.

This covenant would not apply to any recapitalization transaction, a change of control affecting us or a highly leveraged transaction, unless the transaction or change of control were structured to include a merger or consolidation or transfer or lease of all or substantially all of our assets.

Events of Default

The indenture provides that the following will be "events of default" with respect to any series of debt securities:

failure to pay interest for 30 days after the date payment is due and payable; provided, however, that a valid extension of the interest payment period in accordance with the indenture will not constitute a failure to pay interest;

failure to pay principal or premium, if any, on any debt security when due, either at maturity, upon any redemption, by declaration or otherwise and, in the case of technical or administrative difficulties, only if such default persists for a period of more than three business days;

any guarantee by any of the Subsidiary Guarantors ceases to be in full force and effect or is declared null and void or any such Subsidiary Guarantor denies that it has any further liability under its guarantee to the note holders, or has given notice to such effect (other than by reason of the termination of the Indenture or the release of such guarantee in accordance with the Indenture), and such condition shall have continued for a period of 30 days after notice is given as specified in the Indenture;

failure to perform other covenants contained in the indenture for the benefit of the debt securities for 75 days after notice is given by the holders of at least 25% in principal amount of the outstanding debt securities of that series or by the trustee as specified in the indenture;

certain events in bankruptcy, insolvency or reorganization relating to us; or

any other event of default provided in the applicable officer's certificate, resolution of our board of directors or the supplemental indenture under which we issue a series of debt securities.

An event of default for a particular series of debt securities does not necessarily constitute an event of default for any other series of debt securities issued under the indenture. For each series of debt securities, any modifications to the above events of default will be described in the applicable prospectus supplement for those debt securities.

The indenture provides that if an event of default specified in the first, second, third or fifth bullets above occurs and is continuing, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series may declare the principal amount of all those debt securities (or, in the case of discount securities or indexed securities, that portion of the principal amount as may be specified in the terms of that series) to be due and payable immediately. If an event of default specified in the fourth bullet above occurs and is continuing, then the principal amount of all those debt securities (or, in the case of discount securities or indexed securities, that portion of the principal amount as may be specified in the terms of that series) will be due and payable immediately, without any declaration or other act on the part of the trustee or any holder. In certain cases, holders of a majority in principal amount of the outstanding debt securities of any series may, on behalf of holders of all those debt securities, rescind and annul a declaration of acceleration.

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The indenture imposes limitations on suits brought by holders of debt securities against us. Except for actions for payment of overdue principal or interest, no holder of debt securities of any series may institute any action against us under the indenture unless:

the holder has previously given to the trustee written notice of default and continuance of such default;

the holders of at least 25% in principal amount of the outstanding debt securities of the affected series have requested that the trustee institute the action;

the requesting holders have offered the trustee indemnity for the reasonable expenses and liabilities that may be incurred by bringing the action;

the trustee has not instituted the action within 60 days of the request and offer of indemnity; and

the trustee has not received inconsistent direction during such 60-day period by the holders of a majority in principal amount of the outstanding debt securities of the affected series.

We will be required to file annually with the trustee a certificate, signed by one of our officers, stating whether or not the officer knows of any default by us in the performance, observance or fulfillment of any condition or covenant of the indenture.

Discharge, Defeasance and Covenant Defeasance

We can discharge or decrease our obligations under the indenture as stated below.

We may discharge obligations to holders of any series of debt securities that have not already been delivered to the trustee for cancellation and that have either become due and payable or are by their terms to become due and payable, or are scheduled for redemption, within one year. We may effect a discharge by irrevocably depositing with the trustee cash or government obligations denominated in the currency of the debt securities, as trust funds, in an amount certified to be enough to pay when due, whether at maturity, upon redemption or otherwise, the principal of, and any premium and interest on, the debt securities and any mandatory sinking fund payments.

Unless otherwise provided in the applicable prospectus supplement, we may also discharge any and all of our obligations to holders of any series of debt securities at any time, which we refer to as defeasance. We may also be released from the obligations imposed by any covenants of any outstanding series of debt securities and provisions of the indenture, and we may omit to comply with those covenants without creating an event of default under the trust declaration, which we refer to as covenant defeasance. We may effect defeasance and covenant defeasance only if, among other things:

we irrevocably deposit with the trustee cash or government obligations denominated in the currency of the debt securities, as trust funds, in an amount certified to be enough to pay at maturity, or upon redemption, the principal (including any mandatory sinking fund payments) of, and any premium and interest on, all outstanding debt securities of the series; and

we deliver to the trustee an opinion of counsel to the effect that the holders of the series of debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the defeasance or covenant defeasance and that defeasance or covenant defeasance will not otherwise alter the holders' U.S. federal income tax treatment of principal, and any premium and interest payments on, the series of debt securities.

In the case of a defeasance by us, the opinion we deliver must be based on a ruling of the Internal Revenue Service issued, or a change in U.S. federal income tax law occurring, after the date of the indenture, since such a result would not occur under the U.S. federal income tax laws in effect on that date.

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Although we may discharge or decrease our obligations under the indenture as described in the two preceding paragraphs, we may not avoid, among other things, our duty to register the transfer or exchange of any series of debt securities, to replace any temporary, mutilated, destroyed, lost or stolen series of debt securities or to maintain an office or agency in respect of any series of debt securities.

Modification of the Indenture

The indenture provides that we and the trustee, and if applicable, any Subsidiary Guarantor, may enter into supplemental indentures without the consent of the holders of debt securities to, among other things:

evidence the assumption by a successor entity of our obligations;

add to our covenants for the benefit of the holders of debt securities, or to surrender any rights or power conferred upon us;

add any additional events of default;

cure any ambiguity or omission or correct any inconsistency or defect in the indenture;

add to, change or eliminate any of the provisions of the indenture in a manner that will become effective only when there is no outstanding debt security which is entitled to the benefit of the provision as to which the modification would apply;

add guarantees or guarantors of or secure any debt securities;

establish the forms or terms of debt securities of any series, including the terms of any Subsidiary Guarantor's guarantee of such debt securities;

evidence and provide for the acceptance of appointment by a successor trustee and add to or change any of the provisions of the indenture as is necessary for the administration of the trusts by more than one trustee;

modify, eliminate or add to the provisions of the indenture as shall be necessary to effect the qualification of the indenture under the Trust Indenture Act of 1939 or under any similar federal statute later enacted, and to add to the indenture such other provisions as may be expressly required by the Trust Indenture Act; and

make any other provisions with respect to matters or questions arising under the indenture that will not be inconsistent with any provision of the indenture as long as the new provisions do not adversely affect the interests of the holders of any outstanding debt securities of any series created prior to the modification in any material respect.

The indenture also provides that we and the trustee may, with the consent of the holders of not less than a majority in aggregate principal amount of debt securities of each series of debt securities affected by such supplemental indenture then outstanding, add any provisions to, or change in any manner, eliminate or modify in any way the provisions of, the indenture, any subsidiary guarantee or any supplemental indenture or modify in any manner the rights of the holders of the debt securities. We and the trustee may not, however, without the consent of the holder of each outstanding debt security affected thereby:

extend the final maturity of any debt security;

reduce the principal amount or premium, if any;

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reduce the rate or extend the time of payment of interest;

reduce the amount of the principal of any debt security issued with an original issue discount that is payable upon acceleration;

change the currency in which the principal, and any premium or interest, is payable;

impair the right to institute suit for the enforcement of any payment on any debt security when due;

if applicable, adversely affect the right of a holder to convert or exchange a debt security; or

reduce the percentage of holders of debt securities of any series whose consent is required for any modification of the indenture or for waivers of compliance with or defaults under the indenture with respect to debt securities of that series.

The indenture provides that the holders of not less than a majority in aggregate principal amount of the then outstanding debt securities of any series, by notice to the relevant trustee, may on behalf of the holders of the debt securities of that series waive any default and its consequences under the indenture except:

a default in the payment of, any premium and any interest on, or principal of, any such debt security held by a nonconsenting holder; or

a default in respect of a covenant or provision of the indenture that cannot be modified or amended without the consent of the holder of each outstanding debt security of each series affected.

Registered Global Securities and Book Entry System

The debt securities of a series may be issued in whole or in part in book-entry form and will be represented by one or more fully registered global securities. We will deposit any registered global securities with a depositary or with a nominee for a depositary identified in the applicable prospectus supplement and registered in the name of such depositary or nominee. In such case, we will issue one or more registered global securities denominated in an amount equal to the aggregate principal amount of all of the debt securities of the series to be issued and represented by such registered global security or securities. This means that we will not issue certificates to each holder.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a registered global security may not be transferred except as a whole:

by the depositary for the registered global security to its nominee;

by a nominee of the depositary to the depositary or another nominee of the depositary; or

by the depositary or its nominee to a successor of the depositary or a nominee of the successor.

The prospectus supplement relating to a series of debt securities will describe the specific terms of the depositary arrangement involving any portion of the series represented by a registered global security. We anticipate that the following provisions will apply to all depositary arrangements for debt securities:

ownership of beneficial interests in a registered global security will be limited to persons that have accounts with the depositary for such registered global security, these persons being referred to as "participants," or persons that may hold interests through participants;

upon the issuance of a registered global security, the depositary for the registered global security will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal amounts of the debt securities represented by the registered global security beneficially owned by the participants;

any dealers, underwriters, or agents participating in the distribution of the debt securities will designate the accounts to be credited; and

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ownership of beneficial interest in the registered global security will be shown on, and the transfer of the ownership interest will be effected only through, records maintained by the depository for the registered global security for interests of participants, and on the records of participants for interests of persons holding through participants.

The laws of some states may require that specified purchasers of securities take physical delivery of the securities in definitive form. These laws may limit the ability of those persons to own, transfer or pledge beneficial interests in registered global securities.

So long as the depository for a registered global security, or its nominee, is the registered owner of the registered global security, the depository or such nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the registered global security for all purposes under the indenture. Except as stated below, owners of beneficial interests in a registered global security:

will not be entitled to have the debt securities represented by a registered global security registered in their names;

will not receive or be entitled to receive physical delivery of the debt securities in the definitive form; and

will not be considered the owners or holders of the debt securities under the relevant indenture.

Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depository for the registered global security and, if the person is not a participant, on the procedures of a participant through which the person owns its interest, to exercise any rights of a holder under the indenture.

We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the indenture, the depository for the registered global security would authorize the participants holding the relevant beneficial interests to give or take the action, and the participants would authorize beneficial owners owning through the participants to give or take the action or would otherwise act upon the instructions of beneficial owners holding through them.

We will make payments of principal and premium, if any, and interest, if any, on debt securities represented by a registered global security registered in the name of a depository or its nominee to the depository or its nominee, as the case may be, as the registered owners of the registered global security. Neither we nor the trustee, or any other agent of ours or the trustee will be responsible or liable for any aspect of the records relating to, or payments made on account of, beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

We expect that the depository for any debt securities represented by a registered global security, upon receipt of any payments of principal and premium, if any, and interest, if any, in respect of the registered global security, will promptly credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the registered global security as shown on the records of the depository. We also expect that standing customer instructions and customary practices will govern payments by participants to owners of beneficial interests in the registered global security held through the participants, as is now the case with the securities held for the accounts of customers in bearer form or registered in "street name." We also expect that any of these payments will be the responsibility of the participants.

If the depository for any debt securities represented by a registered global security is at any time unwilling or unable to continue as depository or stops being a clearing agency registered under the Exchange Act, we will appoint an eligible successor depository. If we fail to appoint an eligible

successor depository within 90 days, we will issue the debt securities in definitive form in exchange for the registered global security. In addition, we may at any time and in our sole discretion decide not to have any of the debt securities of a series represented by one or more registered global securities. In that event, we will issue debt securities of the series in a definitive form in exchange for all of the registered global securities representing the debt securities. The trustee will register any debt securities issued in definitive form in exchange for a registered global security in the name or names as the depository, based upon instructions from its participants, shall instruct the trustee.

We may also issue bearer debt securities of a series in the form of one or more global securities, referred to as "bearer global securities." We will deposit these securities with a depository identified in the prospectus supplement relating to the series. The prospectus supplement relating to a series of debt securities represented by a bearer global security will describe the applicable terms and procedures. These will include the specific terms of the depository arrangement and any specific procedures for the issuance of debt securities in definitive form in exchange for a bearer global security, in proportion to the series represented by a bearer global security.

Concerning the Trustee

The indenture provides that there may be more than one trustee under the indenture, each for one or more series of debt securities. If there are different trustees for different series of debt securities, each trustee will be a trustee of a trust under the indenture separate and apart from the trust administered by any other trustee under that indenture. Except as otherwise indicated in this prospectus or any prospectus supplement, any action permitted to be taken by a trustee may be taken by such trustee only on the one or more series of debt securities for which it is the trustee under the indenture. Any trustee under the indenture may resign or be removed from one or more series of debt securities. All payments of principal of, and any premium and interest on, and all registration, transfer, exchange, authentication and delivery of, the debt securities of a series will be effected by the trustee for that series at an office designated by the trustee in New York, New York.

The indenture provides that, except during the continuance of an event of default, the trustee will perform only such duties as are specifically set forth in the indenture. During the existence of an event of default, the trustee will exercise those rights and powers vested in it under the indenture and use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

If the trustee becomes a creditor of ours, the indenture places limitations on the right of the trustee to obtain payment of claims or to realize on property received in respect of any such claim as security or otherwise. The trustee may engage in other transactions. If it acquires any conflicting interest relating to any duties concerning the debt securities, however, it must eliminate the conflict or resign as trustee.

No Individual Liability of Incorporators, Shareholders, Officers or Directors

The indenture provides that no past, present or future director, officer, shareholder or employee of ours, any of our affiliates, or any successor corporation, in their capacity as such, shall have any individual liability for any of our obligations, covenants or agreements under the debt securities or the indenture.

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.

DESCRIPTION OF GUARANTEES

This section summarizes some of the terms of the guarantees by any applicable Subsidiary Guarantor. Most of the financial terms and other specific material terms of any guarantees that we offer will be described in a prospectus supplement or term sheet to be attached to the front of this prospectus. Furthermore, since the terms of specific guarantees may differ from the general information provided below, you should rely on information in the prospectus supplement or term sheet if it contradicts information below.

Each guarantee by any Subsidiary Guarantor may:

create a direct obligation of such Subsidiary Guarantor on the debt securities guaranteed, permitting such Subsidiary Guarantor to make payments of principal and interest on such debt securities regardless of whether an event of default has occurred with respect to the issuer of such debt securities;

be senior obligations of the relevant Subsidiary Guarantor in the case of senior debt securities;

be the unsecured and unsubordinated obligations of the relevant Subsidiary Guarantor in the case of senior unsecured debt securities;

rank equally (or pari passu) with all other existing and future unsubordinated and unsecured indebtedness of the relevant Subsidiary Guarantor, respectively in the case of senior unsecured debt securities; and

with respect to any series of debt securities that is designated as subordinated, be junior and subordinated to any guarantee of any senior indebtedness on the same basis as such debt securities are junior and subordinated to any senior indebtedness.

The obligations of each Subsidiary Guarantor under its guarantee will be limited as necessary to prevent that guarantee from constituting a fraudulent conveyance or fraudulent transfer under applicable law.

DESCRIPTION OF SHARE CAPITAL

The following description summarizes the most important terms of our share capital. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our amended and restated memorandum and articles of association, a copy of which has been filed with the SEC, and the applicable provisions of the Companies Law, 2013 Revision, as amended (the "Companies Law").

General

As of the date of this registration statement, we are authorized to issue 200,000,000 ordinary shares, par value \$0.00001 per share, and 230,000 preferred shares, par value \$0.00001 per share. As of April 30, 2015 there were 33,801,727 ordinary shares outstanding, held of record by 129 shareholders, although we believe that there may be a significantly larger number of beneficial owners of our ordinary shares. As of April 30, 2015 there were no preferred shares outstanding.

Meetings of Shareholders

Subject to our regulatory requirements, an annual general meeting and any extraordinary general meeting shall be called by not less than ten days' nor more than 60 days' notice. Notice of every general meeting will be given to all of our shareholders, our directors and our principal external auditors. Extraordinary general meetings may be called only by the chairman of our board of directors, the chief executive officer or a majority of our board of directors, and may not be called by any other person.

Alternatively, subject to applicable regulatory requirements, a meeting will be deemed to have been duly called if it is so agreed (i) in the case of a meeting called as an annual general meeting, by all of our shareholders (or their proxies) entitled to attend and vote at the meeting, or (ii) in the case of an extraordinary meeting, by a majority in number of our shareholders (or their proxies) having a right to attend and vote at the meeting, being a majority together holding not less than 95% of the voting shares.

At any general meeting, shareholders entitled to vote and present in person or by proxy that represent not less than a majority of our issued and outstanding voting shares will constitute a quorum. No business may be transacted at any general meeting unless a quorum is present at the commencement of business.

A corporation being a shareholder shall be deemed for the purpose of our amended and restated memorandum and articles of association to be present in person if represented by its duly authorized representative being the person appointed by resolution of the directors or other governing body of such corporation to act as its representative at the relevant general meeting or at any relevant general meeting of any class of our shareholders. Such duly authorized representative shall be entitled to exercise the same powers on behalf of the corporation which he represents as that corporation could exercise if it were an individual shareholder.

The quorum for a separate general meeting of the holders of a separate class of shares is described in "Modification of Rights" below.

Voting Rights Attaching to the Shares

Subject to any special rights or restrictions as to voting then attached to any shares, at any general meeting every shareholder who is present in person or by proxy (or, in the case of a shareholder being a corporation, by its duly authorized representative) shall have one vote per ordinary share. The holders of preferred shares shall have limited voting rights as set out in our amended and restated memorandum and articles of association.

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No shareholder shall be entitled to vote or be deemed to be part of a quorum, in respect of any share, unless such shareholder is registered as our shareholder at the applicable record date for that meeting and all calls or installments due by such shareholder to us, if any, have been paid.

If a clearing house or depository (or its nominee(s)) is our shareholder, it may authorize such person or persons as it thinks fit to act as its representative(s) at any meeting or at any meeting of any class of shareholders, provided that, if more than one person is so authorized, the authorization shall specify the number and class of shares in respect of which each such person is so authorized. A person authorized pursuant to this provision is entitled to exercise the same powers on behalf of the recognized clearing house or depository (or its nominee(s)) as if such person was the registered holder of our shares held by that clearing house or depository (or its nominee(s)), including the right to vote individually on a show of hands.

While there is nothing under the laws of the Cayman Islands that specifically prohibits or restricts the creation of cumulative voting rights for the election of our directors, unlike the requirement under Delaware law that cumulative voting for the election of directors is permitted only if expressly authorized in the certificate of incorporation, it is not a concept that is accepted as a common practice in the Cayman Islands, and we have made no provisions in our amended and restated memorandum and articles of association to allow cumulative voting for such elections.

Protection of Minority Shareholders

The Grand Court of the Cayman Islands may, on the application of shareholders holding not less than one fifth of our shares in issue, appoint an inspector to examine our affairs and report thereon in a manner as the Grand Court shall direct.

Any shareholder may petition the Grand Court of the Cayman Islands which may make a winding up order, if the court is of the opinion that it is just and equitable that we should be wound up.

Claims against us by our shareholders must, as a general rule, be based on the general laws of contract or tort applicable in the Cayman Islands or their individual rights as shareholders as established by our amended and restated memorandum and articles of association.

Our Cayman Islands counsel, Maples and Calder, is not aware of any reported class action having been brought in a Cayman Islands court. Derivative actions have been brought in the Cayman Islands courts, and the Cayman Islands courts have confirmed the availability for such actions. In most cases, the company will be the proper plaintiff in any claim based on a breach of duty owed to it, and a claim against (for example) the company's officers or directors usually may not be brought by a shareholder. However, based on English authorities, which would in all likelihood be of persuasive authority and be applied by a court in the Cayman Islands, exceptions to the foregoing principle apply in circumstances in which:

a company is acting, or proposing to act, illegally or beyond the scope of its authority;

the act complained of, although not beyond the scope of the authority, could be effected if duly authorized by more than the number of votes which have actually been obtained; or

those who control the company are perpetrating a "fraud on the minority."

A shareholder may have a direct right of action against the company where the individual rights of that shareholder have been infringed or are about to be infringed.

Pre-emption Rights

There are no pre-emption rights applicable to the issue of new shares under either Cayman Islands law or our amended and restated memorandum and articles of association.

Liquidation Rights

Subject to any special rights, privileges or restrictions as to the distribution of available surplus assets on liquidation applicable to any class or classes of shares (i) if we are wound up and the assets available for distribution among our shareholders are more than sufficient to repay the whole of the capital paid up at the commencement of the winding up, the excess shall be distributed pari passu among our shareholders in proportion to the amount paid up at the commencement of the winding up on the shares held by them, respectively, and (ii) if we are wound up and the assets available for distribution among our shareholders as such are insufficient to repay the whole of the paid-up capital, those assets shall be distributed so that, as nearly as may be, the losses shall be borne by our shareholders in proportion to the capital paid up at the commencement of the winding up on the shares held by them, respectively.

If we are wound up, the liquidator may with the sanction of an ordinary resolution and any other sanction required by the Companies Law, divide among our shareholders in specie or kind the whole or any part of our assets (whether they shall consist of assets of the same kind or not) and may, for such purpose, set such value as the liquidator deems fair upon any assets to be divided and may determine how such division shall be carried out as between the shareholders or different classes of shareholders. The liquidator may also, with the sanction of an ordinary resolution, vest any part of these assets in trustees upon such trusts for the benefit of our shareholders as the liquidator shall think fit, but so that no shareholder will be compelled to accept any assets, shares or other securities upon which there is a liability.

Modification of Rights

Except with respect to share capital (as described below), alterations to our amended and restated memorandum and articles of association may only be made by special resolution of no less than two-thirds of votes cast at a meeting of our shareholders at which a quorum is present.

Subject to the Companies Law and our amended and restated memorandum and articles of association, all or any of the special rights attached to shares of any class (unless otherwise provided for by the terms of issue of the shares of that class) may be varied, modified or abrogated with the sanction of a resolution passed by a majority of not less than two-thirds of the votes cast passed at a separate meeting of the holders of the shares of that class at which a quorum is present. The provisions of our amended and restated memorandum and articles of association relating to general meetings shall apply similarly to every such separate general meeting, but so that the quorum for the purposes of any such separate general meeting or at its adjourned meeting shall be a person or persons together holding (or represented by proxy) not less than a majority in nominal value of the issued shares of that class, every holder of shares of the class shall be entitled on a poll to one vote for every such share held by such holder and that any holder of shares of that class present in person or by proxy may demand a poll.

The special rights conferred upon the holders of any class of shares shall not, unless otherwise expressly provided in the rights attaching to or the terms of issue of such shares, be deemed to be varied by the creation or issue of further shares with the same rights and privileges.

Alteration of Capital

We may from time to time by ordinary resolution:

increase our capital by such sum, to be divided into shares of such amounts, as the resolution shall prescribe;

consolidate and divide all or any of our share capital into shares of larger amount than our existing shares;

cancel any shares which at the date of the passing of the resolution have not been taken or agreed to be taken by any person, and diminish the amount of our share capital by the amount of the shares so cancelled, subject to the provisions of the Companies Law;

subdivide our shares or any of them into shares of a smaller amount than is fixed by our amended and restated memorandum and articles of association, subject to the Companies Law, and so that the resolution whereby any share is subdivided may determine that, as between the holders of the share resulting from such subdivision, one or more of the shares may have any such preference or other special rights over, or may have such deferred rights or be subject to any such restrictions as compared with, the others as we have power to attach to unissued or new shares; and

divide shares into several classes and without prejudice to any special rights previously conferred on the holders of existing shares, attach to the shares respectively as preferential, deferred, qualified or special rights, privileges, conditions or such restrictions which in the absence of any such determination in general meeting may be determined by our directors.

We may, by special resolution, subject to any confirmation or consent required by the Companies Law, reduce our share capital or any capital redemption reserve in any manner authorized by law.

Transfer of Shares

Subject to any applicable restrictions set forth in our amended and restated memorandum and articles of association, any of our shareholders may transfer all or a portion of their shares by an instrument of transfer in the usual or common form or in a form prescribed by the Nasdaq Global Market or in any other form which our directors may approve.

Our directors may, in their absolute discretion, decline to register any transfer of shares, subject to any applicable requirements imposed from time to time by the Securities and Exchange Commission, the Nasdaq Global Market or any recognized stock exchange on which our securities are listed. If our directors refuse to register a transfer, they shall, within two months after the date on which the instrument of transfer was lodged, send to each of the transferor and the transferee notice of such refusal.

The registration of transfers may be suspended and the register closed at such times and for such periods as our directors may from time to time determine; provided, however, that registration shall not be suspended for more than forty-five days in any year.

Share Repurchase

We are empowered by the Companies Law and our amended and restated memorandum and articles of association to purchase our own shares, subject to certain restrictions. Our directors may only exercise this power on our behalf, subject to the Companies Law, our amended and restated memorandum and articles of association and to any applicable requirements imposed from time to time by the Securities and Exchange Commission, the Nasdaq Global Market or any recognized stock exchange on which our securities are listed.

Dividends

Subject to the Companies Law, we may declare dividends in any currency to be paid to our shareholders but no dividend shall be declared in excess of the amount recommended by our directors. Dividends may be declared and paid out of our profits, realized or unrealized, or from any reserve set aside from profits that our directors determine is no longer needed. Our board of directors may also declare and pay dividends out of the share premium account or any other fund or account which can be authorized for this purpose in accordance with the Companies Law.

Governance Agreement

The Governance Agreement by and between Glaxo Group Limited and us, dated March 3, 2014 (the "Governance Agreement") contains agreements relating to future acquisitions or dispositions and voting of our securities by GSK, and exempts GSK from triggering our rights agreement until December 31, 2017 (as further described under "Rights Agreement" below), among other matters. Except as otherwise noted below, the provisions of the Governance Agreement described below will terminate at the earliest of (i) when GSK beneficially owns 100% of our outstanding voting shares, (ii) the effective time of a change in control of us and (iii) December 31, 2017.

Voting Arrangements

GSK has agreed to vote the voting shares held by them (at their election) either (i) in accordance with the recommendation of our independent directors or (ii) in proportion to the votes cast by the other holders of our voting shares; however, GSK can vote as it chooses on any matter involving:

any proposal to issue equity securities to one or more parties (other than in a public offering) that would result in that party or parties owning or having the right to acquire 20% or more of the aggregate voting power of all of our equity securities; or

a change in control of us.

In addition, for so long as GSK owns 50.1% or more of our voting shares, it can also vote as it chooses on any matter involving:

an acquisition by us of any business or assets that would constitute a substantial portion of our business or our assets; or

the sale, lease, license, transfer or otherwise disposal of all or a substantial portion of our business or our assets (other than a sale, lease, license or transfer of assets in the ordinary course of our business).

If a person or group acquires 20% or more of our voting shares, GSK may vote its voting shares without any restrictions. GSK has granted an irrevocable proxy coupled with an interest in all voting shares owned by them to our board of directors. This proxy will enable the proxyholder to vote or otherwise act with respect to all of the voting shares of GSK in the manner required by the Governance Agreement.

Limitations and Exceptions to Rights to Acquire Our Securities

Limitation on Acquisition of Our Equity Securities

Except as expressly permitted by the Governance Agreement or as agreed to by us in writing following approval by a majority of our independent directors, GSK may not, directly or indirectly:

acquire any of our equity securities;

make or participate in any solicitation of proxies to vote from any holders of our equity securities;

form or participate in a group with any person not bound by the terms of the Governance Agreement (other than GSK's affiliates) with respect to any of our voting shares;

acquire any of our assets or rights to purchase any of our assets except for assets offered for sale by us;

enter into any arrangement or understanding with others to do any of the actions listed immediately above; or

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act in concert with others to offer to us or any of our shareholders any business combination, restructuring, recapitalization or similar transaction involving us or otherwise seek in concert with others to control, change or influence the management, board of directors or our policies or nominate any person as a director who is not nominated by the then incumbent directors, or propose any matter to be voted upon by our shareholders.

Permitted Purchases of Our Equity Securities from Us

GSK may acquire our equity securities from us in the following circumstances:

if we issue equity securities to a third party (other than equity awards issued as compensation to our directors, officers, employees or consultants), including securities offered by this prospectus, GSK has rights to advance notice and to purchase from us all or a portion of the number of equity securities that would bring their percentage ownership of our voting shares to the same level that it was at immediately prior to the issuance of equity securities to the third party at the same price at which the equity securities were sold to the third party;

the purchase, on a quarterly basis, of equity securities comparable to those that are issued as compensation to our directors, officers, employees or consultants during the preceding quarter pursuant to option exercises, settlement of restricted stock unit awards and vesting of restricted stock, at the fair market value at the time of GSK's notification to us of its intention to purchase such equity securities that would bring their percentage ownership of our voting shares to the same level that it was at immediately prior to such issuances or vesting;

the acquisition of additional equity securities issued in connection with a share split or recapitalization; and

the purchase of equity securities for a pension plan or benefit plan for the benefit of GSK's employees.

Permitted Purchases of Equity Securities from Our Shareholders

GSK may acquire our equity securities from our shareholders in the following circumstances:

the acquisition of securities of another biotechnology or pharmaceutical company that owns our equity securities (provided that those shares will be subject to the provisions of the Governance Agreement); or

the making of an offer to acquire equity securities if (i) a person or group (other than GSK) acquires 20% or more of our voting shares or (ii) our board of directors formally takes certain actions to facilitate a change in control of us (other than with GSK), subject to the following conditions:

that the offer be an offer for 100% of our voting shares;

that the offer include no condition as to financing; and

that the offer includes a condition that the holders of a majority of the voting shares not owned by GSK accept the offer by tendering their shares or voting their shares in favor of the offer.

The term "change in control" is referred to as (i) any transaction or series of related transactions (including mergers, consolidations and other forms of business consolidations) after which our continuing shareholders hold less than 50% of the outstanding voting securities of either us or the entity that survives the transaction (or the parent of the surviving entity) or (ii) subject to certain exceptions, the sale, lease, license, transfer or other disposal of all or substantially all of our business or assets other than to our majority owned and controlled subsidiaries.

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The term "equity securities" is referred to as (i) any of our voting shares, (ii) our securities convertible into or exchangeable for voting shares, and (iii) options, rights and warrants issued by us to acquire voting shares.

Registration Rights Agreement

Ordinary shares issued to GSK are entitled to the rights set forth in the Registration Rights Agreement by and between GSK and us, dated March 3, 2014 (the "Registration Rights Agreement"). The rights under the Registration Rights Agreement will expire on December 31, 2024, or if GSK or its permitted assigns each hold one and a half percent or less of our then outstanding ordinary shares, if each such holder can sell its shares in a single transaction pursuant to Rule 144 under the Securities Act.

Demand Registration Rights

Under the Registration Rights Agreement, GSK and its permitted assigns have the right to require that we register their ordinary shares, provided such demand comes from holders of at least 50% of the aggregate shares held by GSK and its permitted assigns and such registration relates to ordinary shares having an anticipated aggregate offering price of \$10 million. We are only obligated to effect one registration in response to these demand registration rights (subject to certain exceptions). We may postpone the filing of a registration statement for up to 90 days once in any 12-month period if our board of directors determines in good faith that the filing would be seriously detrimental to our shareholders or us. The underwriters of any underwritten offering have the right to limit the number of shares to be included in a registration statement filed in response to the exercise of these demand registration rights. We must pay all expenses, except for underwriters' discounts and commissions, incurred in connection with these demand registration rights.

Piggyback Registration Rights

If we register any securities for public sale, under the Registration Rights Agreement GSK has the right to include its shares in the registration, subject to specified exceptions. The underwriters of any underwritten offering have the right to limit the number of shares registered by GSK and its permitted assigns (but to no less than 25% of the shares to be registered in such registration) due to marketing reasons. We must pay all expenses, except for underwriters' discounts and commissions, incurred in connection with these piggyback registration rights.

S-3 Registration Rights

While we are eligible to file a registration statement on Form S-3, under the Registration Rights Agreement GSK and its permitted assigns can request that we register their shares, provided that such registration request is made by holders of not less than 10% in aggregate of GSK's and its permitted assigns shares and the total price of the ordinary shares offered to the public is at least \$10 million. GSK and its permitted assigns may only require us to file two Form S-3 registration statements in any 12-month period. We may postpone the filing of a Form S-3 registration statement for up to 90 days once in any 12-month period if our board of directors determines in good faith that the filing would be seriously detrimental to our shareholders or us. We must pay all expenses, except for underwriters' discounts and commissions, incurred in connection with these F-3 registration rights.

Rights Agreement

Under our rights agreement, each ordinary share has associated with it one preferred share purchase right. Each of these rights entitles its holder to purchase, at a price of \$225.00 for each, one one-thousandth of a share of Series A junior participating preferred, (each subject to adjustment) under circumstances provided for in the rights agreement. The purpose of our rights agreement is to:

give our board of directors the opportunity to negotiate with any persons seeking to obtain control of us;

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deter acquisitions of voting control of us without assurance of fair and equal treatment of all of our shareholders; and

prevent a person from acquiring in the market a sufficient amount of voting power over us to be in a position to block an action sought to be taken by our shareholders.

The exercise of the rights under our rights agreement would cause substantial dilution to a person attempting to acquire us on terms not approved by our board of directors, and therefore would significantly increase the price that such person would have to pay to complete the acquisition. Our rights agreement may deter a potential acquisition or tender offer. Until a "distribution date" occurs, the rights will:

not be exercisable;

be represented in the same book-entry form or by the same certificate that represents the shares with which the rights are associated; and

trade together with those shares.

The rights will expire at the close of business on May 24, 2024, unless earlier redeemed or exchanged by us. Following a "distribution date," the rights would become exercisable and we would issue separate certificates representing the rights, which would trade separately from our ordinary shares. A "distribution date" would occur upon the earlier of:

ten business days after a public announcement that the person has become an "acquiring person;" or

ten business days (or such later date as may be determined by action of the board of directors prior to such time as any person or group of affiliated persons becomes an "acquiring person") after the commencement of, or announcement of an intention to make, a tender offer or exchange offer the consummation of which would result in the beneficial ownership by a person or group of 19% or more of the outstanding ordinary shares.

A holder of rights will not, as such, have any rights as a shareholder, including the right to vote or receive dividends.

Under our rights agreement, a person becomes an "acquiring person" if the person, alone or together with a group, acquires beneficial ownership of 19% or more of our outstanding ordinary shares. GSK is not an "acquiring person" because we have, pursuant to our governance agreement with GSK, exempted GSK from the application of our rights agreement. In addition, an "acquiring person" shall not include us, any of our subsidiaries, or any of our employee benefit plans or any person or entity acting pursuant to such employee benefit plans. Our rights agreement also contains provisions designed to prevent the inadvertent triggering of the rights by institutional or certain other shareholders.

If any person becomes an acquiring person, each holder of a right, other than the acquiring person, will be entitled to purchase, at the purchase price, a number of our ordinary shares having a market value of two times the purchase price. If, following a public announcement that a person has become an acquiring person:

we merge or enter into any similar business combination transaction and we are not the surviving corporation; or

50% or more of our assets, cash flow or earning power is sold or transferred,

each holder of a right, other than the acquiring person, will be entitled to purchase a number of ordinary shares of the surviving entity having a market value of two times the purchase price.

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After a person becomes an acquiring person, but prior to such person acquiring 50% of our outstanding ordinary shares, our board of directors may exchange each right, other than rights owned by the acquiring person, for

one ordinary share;

one one-thousandth of a share of our Series A junior preferred share; or

a fractional share of another series of preferred share having equivalent value.

At any time until a person has become an acquiring person, our board of directors may redeem all of the rights at a redemption price of \$0.01 per right. On the redemption date, the rights will expire and the only entitlement of the holders of rights will be to receive the redemption price.

For so long as the rights are redeemable, our board of directors may amend any provisions in the rights agreement without shareholder consent. After the rights are no longer redeemable, our board of directors may only amend the rights agreement without shareholder consent if such amendment would not change the amendment provisions, adversely affect the interests of the holders of rights, or cause the rights to again become redeemable. Despite the foregoing, at no time may the redemption price of the rights be amended or changed.

The adoption of the rights agreement and the distribution of the rights should not be taxable to our shareholders or us. Our shareholders may recognize taxable income when the rights become exercisable in accordance with the rights agreement.

Differences in Corporate Law

The Companies Law is modeled after similar laws in the United Kingdom but does not follow recent changes in United Kingdom laws. In addition, the Companies Law differs from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of the significant differences between the provisions of the Companies Law applicable to us and the laws applicable to companies incorporated in the United States and their shareholders.

Mergers and Similar Arrangements

The Companies Law permits mergers and consolidations between Cayman Islands companies and between Cayman Islands companies and non-Cayman Islands companies.

For these purposes, (a) "merger" means the merging of two or more constituent companies and the vesting of their undertaking, property and liabilities in one of such companies as the surviving company and (b) a "consolidation" means the combination of two or more constituent companies into a consolidated company and the vesting of the undertaking, property and liabilities of such companies to the consolidated company. In order to effect such a merger or consolidation, the directors of each constituent company must approve a written plan of merger or consolidation, which must then be authorized by a special resolution of the shareholders of each constituent company and such other authorization, if any, as may be specified in such constituent company's articles of association. The plan must be filed with the Registrar of Companies together with a declaration as to the solvency of the consolidated or surviving company, a list of the assets and liabilities of each constituent company and an undertaking that a copy of the certificate of merger or consolidation will be given to the members and creditors of each constituent company and published in the Cayman Islands Gazette.

Dissenting shareholders have the right to be paid the fair value of their shares (which, if not agreed between the parties, will be determined by the Cayman Islands court) if they follow the required procedures, subject to certain exceptions. Court approval is not required for a merger or consolidation which is effected in compliance with these statutory procedures.

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In addition, there are statutory provisions that facilitate the reconstruction and amalgamation of companies, provided that the arrangement in question is approved by a majority in number representing 75% in value of each class of shareholders and creditors with whom the arrangement is to be made that are present and voting either in person or by proxy at a meeting, or meetings convened for that purpose. The convening of the meetings and subsequently the arrangement must be sanctioned by the Grand Court of the Cayman Islands. While a dissenting shareholder would have the right to express to the court the view that the transaction should not be approved, the court can be expected to approve the arrangement if it satisfies itself that:

we are not proposing to act illegally or ultra vires and the statutory provisions as to majority vote have been complied with;

the shareholders have been fairly represented at the meeting in question;

the arrangement is such as a businessman would reasonably approve; and

the arrangement is not one that would more properly be sanctioned under some other provision of the Companies Law or that would amount to a "fraud on the minority."

When a takeover offer is made and accepted by holders of at least 90% of the shares within four months, the offeror may, within a two-month period, require the holders of the remaining shares to transfer such shares on the terms of the offer. An objection may be made to the Grand Court of the Cayman Islands but is unlikely to succeed unless there is evidence of fraud, bad faith or collusion.

If the arrangement and reconstruction are thus approved, any dissenting shareholders would have no rights comparable to appraisal rights, which might otherwise ordinarily be available to dissenting shareholders of U.S. corporations and allow such dissenting shareholders to receive payment in cash for the judicially determined value of their shares.

Shareholders' Suits

We are not aware of any reported class action or derivative action having been brought in a Cayman Islands court. However, a class action suit could nonetheless be brought in a U.S. court pursuant to an alleged violation of U.S. securities laws and regulations. Our Cayman Islands counsel, Maples and Calder, is not aware of any reported class action having been brought in a Cayman Islands court. Derivative actions have been brought in the Cayman Islands courts, and the Cayman Islands courts have confirmed the availability for such actions. In most cases, the company will be the proper plaintiff in any claim based on a breach of duty owed to it, and a claim against (for example) the company's officers or directors usually may not be brought by a shareholder. However, based on English authorities, which would in all likelihood be of persuasive authority and be applied by a court in the Cayman Islands, exceptions to the foregoing principle apply in circumstances in which:

a company is acting, or proposing to act, illegally or beyond the scope of its authority;

the act complained of, although not beyond the scope of the authority, could be effected if duly authorized by more than the number of votes which have actually been obtained; or

those who control the company are perpetrating a "fraud on the minority."

A shareholder may have a direct right of action against the company where the individual rights of that shareholder have been infringed or are about to be infringed.

Corporate Governance

Cayman Islands laws do not restrict transactions with directors, requiring only that directors exercise a duty of care and owe fiduciary duties to the companies for which they serve. Under our amended and restated memorandum and articles of association, subject to any separate requirement for

audit committee approval under the applicable rules of the Nasdaq Global Market or unless disqualified by the chairman of the relevant board meeting, so long as a director discloses the nature of his interest in any contract or arrangement which he is interested in, such a director may vote in respect of any contract or proposed contract or arrangement in which such director is interested and may be counted in the quorum at such meeting.

Board of Directors

We are managed by our board of directors. Our amended and restated memorandum and articles of association will provide that the number of our directors will be fixed from time to time by our board of directors but may not consist of less than three or more than 15 directors. Each director holds office until the expiration of his or her term in accordance with the terms of our amended and restated memorandum and articles of association, until his or her successor has been duly elected and qualified or until his or her death, resignation or removal. Our directors may only be removed for cause by our board of directors. Any vacancies on our board of directors or additions to the existing board of directors can only be filled by the affirmative vote of a simple majority of the remaining directors, although this may be less than a quorum. Any director so appointed by the board of directors shall hold office only for the remaining term of the class of director which he or she replaces and shall then be eligible for re-election. Our directors are not required to hold any of our shares to be qualified to serve on our board of directors.

Meetings of our board of directors may be convened at any time deemed necessary by our secretary on request of the chairman of our board of directors, our chief executive officer, if not the chairman of our board of directors, or a majority of our board of directors. Advance notice of a meeting is not required if each director entitled to attend consents to the holding of such meeting.

Issuance of Additional Ordinary Shares or Preferred Shares

Our amended and restated memorandum and articles of association authorize our board of directors to issue additional ordinary shares from time to time as our board of directors shall determine, to the extent available, authorized but unissued shares. The issuance of additional ordinary shares may, subject to applicable law, be used as an anti-takeover device without further action on the part of our shareholders. Such issuance may dilute the voting power of existing holders of ordinary shares.

Our board of directors may authorize by resolution or resolutions from time to time the issuance of one or more classes or series of preferred shares and to fix the designations, powers, preferences and relative, participating, optional and other rights, if any, and the qualifications, limitations and restrictions thereof, if any, including, without limitation, the number of shares constituting each such class or series, dividend rights, conversion rights, redemption privileges, voting powers, full or limited or no voting powers, and liquidation preferences, and to increase or decrease the size of any such class or series (but not below the number of shares of any class or series of preferred shares then outstanding) to the extent permitted by applicable law. The resolution or resolutions providing for the establishment of any class or series of preferred shares may, to the extent permitted by applicable law, provide that such class or series shall be superior to, rank equally with or be junior to the preferred shares of any other class or series. Additionally, the issuance of preference shares may have the effect of decreasing the market price of the ordinary shares and may adversely affect the voting and other rights of the holders of ordinary shares.

Our board of directors may issue series of preferred shares without action by our shareholders to the extent authorized but unissued. Accordingly, the issuance of preferred shares may adversely affect the enjoyment of the rights of the holders of our ordinary shares. In addition, the issuance of preferred shares may be used as an anti-takeover device without further action on the part of our shareholders, subject to applicable law. Issuance of preferred shares may dilute the voting power of holders of ordinary shares.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of debt securities, ordinary shares, or any combination thereof. We may issue warrants independently or together with any other securities offered by any prospectus supplement and may be attached to or separate from the other offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into by us with a warrant agent. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. Further terms of the warrants and the applicable warrant agreements will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement relating to any particular issue of warrants will describe the terms of the warrants, including, as applicable, the following:

the title of the warrants;

the aggregate number of the warrants;

the price or prices at which the warrants will be issued;

the designation, terms and number of ordinary shares or principal amount of debt securities purchasable upon exercise of the warrants;

the designation and terms of the offered securities, if any, with which the warrants are issued and the number of the warrants issued with each offered security;

the date, if any, on and after which the warrants and the related debt securities or ordinary shares will be separately transferable;

the price at which each ordinary share or underlying debt securities purchasable upon exercise of the warrants may be purchased or the manner of determining such price;

the date on which the right to exercise the warrants shall commence and the date on which that right shall expire;

the minimum or maximum amount of the warrants which may be exercised at any one time;

information with respect to book- entry procedures, if any;

a discussion of certain federal income tax considerations; and

any other material terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Before the exercise of warrants to purchase debt securities, holders of such warrants will not be entitled to payments of principal of, premium, if any, or interest, if any, on the debt securities purchasable upon exercise of the warrants, or to enforce any of the covenants in the indenture. Holders of warrants to purchase equity securities will not be entitled, solely by virtue of being holders, to vote, to consent, to receive dividends, to receive notice as shareholders with respect to any meeting of shareholders for the election of directors or any other matter, or to exercise any rights whatsoever as a holder of the equity securities purchasable upon exercise of such warrants.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus to one or more underwriters or dealers for public offering and sale by them or to investors directly or through agents. The prospectus supplement or term sheet will set forth the terms of the offering and the method of distribution and will identify any firms acting as underwriters, dealers or agents in connection with the offering, including:

the name or names of any underwriters, dealers or agents;

the purchase price of the securities and the proceeds to us from the sale; and

any securities exchange or market on which the securities offered in the prospectus supplement may be listed.

Only those underwriters identified in such prospectus supplement are deemed to be underwriters in connection with the securities offered in the prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, or at prices determined as the applicable prospectus supplement specifies. The securities may be sold through a rights offering, forward contracts or similar arrangements. In connection with the sale of the securities, underwriters, dealers or agents may be deemed to have received compensation from us in the form of underwriting discounts or commissions and also may receive commissions from securities purchasers for whom they may act as agent. Underwriters may sell the securities to or through dealers, and the dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agent. Some of the underwriters, dealers or agents who participate in the securities distribution may engage in other transactions with, and perform other services for, us or our subsidiaries in the ordinary course of business.

LEGAL MATTERS

Certain legal matters relating to the issuance of the securities offered by this prospectus will be passed upon for us by Maples and Calder, Cayman Islands, and Shearman & Sterling LLP, San Francisco, 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

Ernst & Young LLP, independent registered public accounting firm, has audited the consolidated financial statements of Theravance Biopharma, Inc. included in the Theravance Biopharma, Inc. Annual Report on Form 10-K for the year ended December 31, 2014, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. The financial statements of Theravance Biopharma, Inc. 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 MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement and any document we file with the SEC at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800- SEC-0330. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site is <http://www.sec.gov>. The information on the SEC's website, other than the documents specifically incorporated by reference herein, is not part of this prospectus, and any references to this website or any other web site are inactive textual references only.

The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus. Information that is incorporated by reference is considered to be part of this prospectus and you should read it with the same care that you read this prospectus. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus, and will be considered to be a part of this prospectus from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus:

The Annual Report on Form 10-K for Theravance Biopharma, Inc. for the fiscal year ended December 31, 2014, filed with the SEC on March 13, 2015 (including the portion of the Proxy Statement on Schedule 14A of Theravance Biopharma, Inc. filed on March 17, 2015, incorporated by reference therein).

The Quarterly Report on Form 10-Q for Theravance Biopharma, Inc. for the quarter ended March 31, 2015, filed on May 13, 2015.

The Current Reports on Form 8-K for Theravance Biopharma, Inc. filed on February 2, 2015, March 9, 2015 and April 24, 2015 and the Current Report on Form 8-K/A for Theravance Biopharma, Inc. filed on April 24, 2015.

The description of ordinary shares contained in the Registration Statement No. 001-36033 on Form 10 filed with the SEC on May 7, 2014, including any amendment or report filed for the purpose of updating such description.

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We also incorporate by reference all additional documents that we file with the SEC under the terms of Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act that are made after the initial filing date of the registration statement of which this prospectus is a part until the offering of the particular securities covered by a prospectus supplement or term sheet has been completed. We are not, however, incorporating, in each case, any documents or information that we are deemed to furnish and not file in accordance with SEC rules.

You may request a copy of any or all of the documents incorporated by reference but not delivered with this prospectus, at no cost, by calling us at (650) 808-6000 or by writing to us at the following address:

Theravance Biopharma, Inc.
c/o Theravance Biopharma US, Inc.
901 Gateway Boulevard
South San Francisco, California 94080
Attn: Investor Relations

Table of Contents

4,765,000 Shares

Theravance Biopharma, Inc.

Ordinary Shares

PROSPECTUS SUPPLEMENT

April 28, 2016

Leerink Partners

Evercore ISI

Guggenheim Securities

Baird
