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Theravance Biopharma annonce que l'étude de phase 3 CYPRESS n'a pas atteint son critère d'évaluation principal ; le conseil d'administration accélère son examen stratégique et annonce des mesures de réduction des coûts

L'étude de phase 3 CYPRESS n'a pas atteint son critère d'évaluation principal, le score composite OHSA, un résultat rapporté par le patient (PRO).

- Trésorerie de 326,5 millions de dollars au T4 2025 (sans dette) ; environ 400 millions de dollars attendus à la fin du T1 2026, y compris la réception des paiements d'étape de 2025 ; Theravance est très confiante d'atteindre l'objectif de 100 millions de dollars du programme TRELEGY en 2026¹.
- Le comité d'examen stratégique accélère ses efforts en cours pour évaluer les alternatives afin de maximiser la valeur actionnariale.
- Restructuration organisationnelle visant à réduire les coûts d'environ 60 % (soit environ 70 millions de dollars). On prévoit que la Société générera un flux de trésorerie annualisé d'environ 60 à 70 millions de dollars.
- Portefeuille rationalisé axé sur YUPELRI®, un produit en croissance pour le traitement de la BPCO, bénéficiant d'une génération de flux de trésorerie durable et d'une protection de la propriété intellectuelle à long terme aux États-Unis jusqu'en 2039 ; chiffre d'affaires net de 266,6 millions de dollars pour l'exercice 2025 comptabilisé par Viatriis (+12 % en glissement annuel)².

DUBLIN, le 3 mars 2026 /PRNewswire/ -- Theravance Biopharma, Inc. (« Theravance Biopharma » ou la « Société ») (NASDAQ : TBPH) a annoncé aujourd'hui les principaux résultats de l'étude de phase 3 **CYPRESS évaluant l'efficacité et la sécurité de l'ampreloxétine chez les patients atteints d'hypotension orthostatique neurogène symptomatique (HON) due à une atrophie multisystémique (AMS), une maladie rare**. L'étude n'a pas atteint son critère d'évaluation principal, à savoir le score composite de l'échelle d'évaluation des symptômes de l'hypotension orthostatique (OHSA). **Suite à ce résultat, la Société a décidé de mettre fin au programme d'ampreloxétine.**

Concernant cette annonce, le Comité d'examen stratégique du Conseil d'administration de Theravance Biopharma (le « Comité ») accélère son examen des solutions alternatives afin de maximiser la valeur pour les actionnaires. Depuis sa création en 2024, le Comité travaille en étroite collaboration avec Lazard, son conseiller financier indépendant, pour évaluer les opportunités offertes à la Société, notamment en fonction des différents scénarios possibles pour l'étude CYPRESS. Fort de ce travail, le Comité examinera rapidement un large éventail de solutions permettant de maximiser la valeur et d'optimiser la fiscalité, y compris, mais sans s'y limiter, une vente de la Société. Rien ne garantit que l'examen stratégique du Comité aboutira à une transaction. Theravance Biopharma n'entend pas divulguer d'autres informations sur cet examen, sauf si elle juge une telle divulgation appropriée ou nécessaire.

Alors que le Comité accélère son examen, Theravance Biopharma met en œuvre une restructuration organisationnelle afin de rationaliser ses coûts et d'aligner ses ressources sur son objectif commercial principal : YUPELRI®. Cette restructuration impliquera la fermeture progressive des activités de R&D et une réduction significative des frais généraux et administratifs. Elle devrait permettre de réduire les charges d'exploitation d'environ 60 % par rapport aux estimations préliminaires de 2025, qui s'élevaient à environ 110 millions de dollars. Les économies réalisées, estimées à environ 70 millions de dollars, devraient se concrétiser pleinement au troisième trimestre 2026.

Grâce aux économies réalisées dans le cadre de cette restructuration et à la poursuite des ventes de YUPELRI®, la société devrait générer un flux de trésorerie annualisé d'environ 60 à 70 millions de dollars à compter du troisième trimestre 2026. Cette prévision de flux de trésorerie comprend un résultat d'exploitation estimé entre 45 et 55 millions de dollars (hors rémunération en actions non monétaire) et des produits financiers et autres produits prévisionnels. Elle n'inclut pas les revenus potentiels liés à l'étape de 100 millions de dollars du projet TRELEGY.

Suite à la décision de mettre fin au programme d'ampreloxétine, les sources de valeur de la Société comprennent environ 400 millions de dollars de trésorerie attendue à la fin du premier trimestre 2026, une participation de 35 % dans YUPELRI® générant un flux de trésorerie durable, le paiement d'étape potentiel lié à TRELEGY, ainsi que des avantages fiscaux irlandais.

« Nous sommes déçus que l'ampreloxétine n'ait pas atteint le critère d'évaluation principal de l'étude CYPRESS. Ces résultats sont particulièrement décourageants pour les patients atteints de cette maladie rare qui espéraient une nouvelle option thérapeutique, ainsi que pour les employés qui ont consacré des années de travail à ce programme. Je tiens à remercier sincèrement les patients, leurs aidants, les investigateurs et notre équipe pour leur engagement et leur contribution à cet effort », a déclaré Rick E. Wunningham, directeur général de Theravance Biopharma. « Au vu de ces résultats, nous prenons des mesures décisives pour restructurer l'organisation et réduire significativement nos coûts, ce qui devrait permettre à YUPELRI® de générer un flux de trésorerie important et durable pour l'entreprise. Grâce à un produit commercial rentable, une trésorerie prévisionnelle d'environ 400 millions de dollars à la fin du premier trimestre 2026 et l'atteinte anticipée du cap de 100 millions de dollars lié à TRELEGY en 2026, nous conservons un solide portefeuille d'actifs. »

« Conformément à notre engagement d'agir au mieux des intérêts de la Société et de ses actionnaires, et parallèlement aux mesures de restructuration annoncées aujourd'hui, le Comité d'examen stratégique accélère son évaluation des options stratégiques permettant d'optimiser la valeur », a déclaré Susannah Gray, présidente indépendante du Conseil d'administration et présidente du Comité d'examen stratégique. « Le Comité a été créé avec un mandat clair : maximiser la valeur pour les actionnaires de Theravance Biopharma. Au cours des dix-huit derniers mois, il s'est activement employé à veiller à ce que la stratégie de la Société atteigne cet objectif, notamment grâce à la vente, en 2025, de notre participation restante dans TRELEGY pour 225 millions de dollars. Aujourd'hui, Theravance Biopharma dispose d'un actif commercial générateur de trésorerie, d'un bilan solide et d'une importante opportunité de versement de dividendes à court terme. Le Comité est pleinement mobilisé pour agir avec diligence et rigueur afin d'obtenir le meilleur résultat possible pour les actionnaires. »

Résultats préliminaires de l'étude de phase 3 CYPRESS

Dans l'étude de phase 3 CYPRESS, le critère d'évaluation principal, à savoir la variation du score composite OHSa à la semaine 8 pendant la période de sevrage randomisée en double aveugle, n'a pas atteint le seuil de signification statistique. Des tendances similaires ont été observées pour les critères d'évaluation secondaires à la semaine 8. Les variations de la pression artérielle, de la fréquence cardiaque et des taux de noradrénaline ont confirmé un effet hypertenseur constant et réaffirmé l'activité biologique de l'amprexétine. L'amprexétine a été généralement bien tolérée, avec un profil de sécurité conforme aux études précédentes, notamment l'absence d'aggravation de l'hypertension en décubitus dorsal.

Alors que la Société poursuit l'arrêt progressif du programme amprexétine, elle réalisera, en consultation avec des experts externes, des analyses complémentaires des données CYPRESS et du programme de phase 3 afin de déterminer si ces données justifient des discussions réglementaires supplémentaires. Cette évaluation vise à apporter au Comité des précisions quant à la valeur résiduelle de l'amprexétine pour les actionnaires de Theravance. Rien ne garantit que des échanges réglementaires supplémentaires auront lieu.

Restructuration organisationnelle

La restructuration devrait toucher environ 50 % des effectifs totaux. Cette réduction comprend la fermeture complète du département R&D et une diminution d'environ 50 % des effectifs administratifs et généraux. Ces mesures seront mises en œuvre au cours des deux prochains trimestres et la société prévoit d'engager des coûts exceptionnels de départ de 5 à 7 millions de dollars liés à ces actions.

Autres faits saillants de la société

YUPELRI® (revefenacin), solution pour inhalation, est le premier et le seul bronchodilatateur LAMA (antagoniste muscarinique à longue durée d'action) nébulisé, à administration unique quotidienne, approuvé aux États-Unis pour le traitement d'entretien des patients atteints de bronchopneumopathie chronique obstructive (BPCO) :

Chiffre d'affaires net trimestriel aux États-Unis de 70,6 millions de dollars au T4 2025, en hausse de 6 % par rapport au T4 2024 (T4 2025 vs T4 2024)³.

Les ventes nettes annuelles aux États-Unis s'élèvent à 266,6 millions de dollars, soit une augmentation de 12 % d'une année sur l'autre (exercice 2025 par rapport à l'exercice 2024), déclenchant un palier de 25 millions de dollars basé sur les ventes de la part de VIATRIS, avec un versement en janvier 2026.

Theravance Biopharma Reports Phase 3 CYPRESS Study Did Not Meet Primary Endpoint; Board Accelerates Strategic Review and Announces Cost Reduction Actions

March 3, 2026 at 8:30 AM EST

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- *Phase 3 CYPRESS study did not meet the primary endpoint, the OHSA Composite Score, a patient reported outcome (PRO)*
- *Cash of \$326.5 million at Q4 2025 (no debt); approximately \$400 million expected at end of Q1 2026 including receipt of 2025 milestones; Theravance highly confident in achieving \$100 million 2026 TRELEGY milestone¹*
- *Strategic Review Committee accelerating ongoing efforts to evaluate alternatives to maximize shareholder value*
- *Organizational restructuring to reduce cost base by approximately 60% (or approximately \$70 million); expected to result in the Company generating approximately \$60 - \$70 million of annualized cash flow*
- *Streamlined portfolio focused on YUPELRI[®], a growing product to treat COPD with durable cash-flow generation and long-dated intellectual property protection in the U.S. into 2039; FY 2025 net sales \$266.6 million recognized by Viatris (+12% YoY)²*

DUBLIN, March 3, 2026 /PRNewswire/ -- Theravance Biopharma, Inc. ("Theravance Biopharma" or the "Company") (NASDAQ: TBPH) today announced topline results from the Phase 3 CYPRESS study evaluating the efficacy and safety of ampreloxetine in patients with symptomatic neurogenic orthostatic hypotension (nOH) due to multiple system atrophy (MSA), a rare disease. The study did not meet its primary endpoint in the Orthostatic Hypotension Symptom Assessment (OHSA) composite score. As a result of this outcome, the Company has decided to wind down the ampreloxetine program.

In connection with this announcement, the Strategic Review Committee of the Theravance Biopharma Board of Directors (the "Committee") is accelerating its ongoing review of alternatives to maximize value for shareholders. Since its formation in 2024, the Committee has been working on an ongoing basis with Lazard, its independent financial advisor, to evaluate opportunities available to the Company, including under multiple potential outcomes for the CYPRESS study. Building upon this work, the Committee will act with urgency to evaluate a broad range of value maximizing and tax efficient alternatives, including but not limited to a sale of the company. There can be no assurance that the Committee's strategic review process will result in any transaction. Theravance Biopharma does not intend to disclose further developments on this review process unless and until it determines that such disclosure is appropriate or necessary.

While the Committee accelerates its review, Theravance Biopharma is implementing an organizational restructuring to streamline costs and align its resources with its commercial focus on YUPELRI[®]. The restructuring will involve winding down the R&D function and significantly reducing the G&A function. The restructuring is expected to reduce operating expenses by approximately 60%, relative to 2025 preliminary actuals of approximately \$110 million. The full run-rate cost savings of approximately \$70 million are expected to fully materialize in the third quarter of 2026.

Together, the cost savings from the restructuring and continued sales from YUPELRI[®] are expected to result in the Company generating approximately \$60 to \$70 million of annualized cash flow, starting in Q3 2026. This cash flow projection is comprised of an estimated \$45 to \$55 million of Income from Operations (excluding non-cash share-based compensation) and projected Interest and Other Income, and does not include potential income from the \$100 million TRELEGY milestone.

Following the decision to wind down the amprelosetine program, the Company's sources of value include approximately \$400 million of expected cash at the end of Q1 2026, a 35% interest in YUPELRI® that generates durable cash flow, and the potential TRELEGY milestone payment, as well as Irish tax attributes.

"We are disappointed that amprelosetine did not meet the primary endpoint in the CYPRESS study. These results are particularly disheartening for the patients who are suffering from this rare disease and were hoping for a new treatment option and for the employees who dedicated years of work to this program. I want to sincerely thank the patients, caregivers, investigators, and our team for their commitment and contributions to this effort," said Rick E Winningham, Chief Executive Officer of Theravance Biopharma. "Given these results, we are taking decisive steps to restructure the organization and significantly reduce our cost base, which we expect will allow YUPELRI® to drive meaningful and sustainable cash flow for the company. With a profitable commercial product, an expected cash balance of approximately \$400 million at the end of the first quarter of 2026, and the anticipated \$100 million TRELEGY milestone in 2026, we continue to have a strong set of assets."

"Consistent with our commitment to act in the best interests of the Company and its shareholders, and alongside the organizational restructuring actions we announced today, the Strategic Review Committee is accelerating its ongoing evaluation of value maximizing strategic alternatives," said Susannah Gray, independent Chair of the Board and Chair of the Strategic Review Committee. "The Committee was established with a clear mandate to deliver maximum value to Theravance Biopharma shareholders, and over the last year and a half, has been actively engaged in overseeing that the Company's strategy delivers on this objective, including with the \$225 million sale of our remaining royalty interest in TRELEGY in 2025. Today, Theravance Biopharma has a cash-generative commercial asset, strong balance sheet and sizable near-term milestone payout opportunity, and the Committee is squarely focused on acting with urgency and discipline to ensure that we achieve the best outcome for shareholders."

Phase 3 CYPRESS Topline Data Study Results

In the Phase 3 CYPRESS study, the primary endpoint, the change in OHSA composite score at Week 8 during the double-blind randomized withdrawal period, was not statistically significant. Similar trends were observed in the secondary endpoints at week 8. Changes in blood pressure, heart rate and norepinephrine levels confirmed a consistent pressor effect and reaffirmed amprelosetine's biological activity. Amprelosetine was generally well tolerated, with safety findings consistent with prior studies, including no signal of worsening of supine hypertension.

As the Company proceeds with the orderly wind down of the amprelosetine program, it will complete additional analyses of the CYPRESS dataset and Phase 3 program, in consultation with external experts, to assess whether the data merits further regulatory discussion. This assessment is intended to provide the Committee with additional clarity regarding any remaining value in amprelosetine for Theravance shareholders. There can be no assurance that any additional regulatory engagement will occur.

Organizational Restructuring

The restructuring is expected to impact approximately 50% of the overall workforce. This reduction includes the complete wind-down of the R&D organization and a decrease of approximately 50% in G&A employees. These actions will be implemented over the next two quarters, and the Company expects to incur approximately \$5 to \$7 million in one-time cash severance costs related to these actions.

Additional Company Highlights

YUPELRI[®] (revefenacin) inhalation solution, the first and only once-daily, nebulized LAMA (long-acting muscarinic antagonist) bronchodilator approved in the U.S. for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD):

- Quarterly U.S. net sales of \$70.6 million in Q4 2025, increasing 6% year-over-year (YoY) (Q4 2025 vs Q4 2024)³.
- Annual U.S. net sales of \$266.6 million, increasing 12% year-over-year (YoY) (FY 2025 vs FY 2024) triggering \$25 million sales-based milestone from VIATRIS with cash received in January 2026.

TRELEGY

- GSK reported FY 2025 global TRELEGY net sales of approximately \$3.91 billion⁴, meeting the threshold for a \$50 million milestone from Royalty Pharma, with cash received in February 2026.
- Company expects FY 2026 global net sales of at least approximately \$3.51 billion, which will trigger an additional \$100 million milestone from Royalty Pharma.

Financial Position

- Cash totaled \$326.5 million as of December 31, 2025, with no debt.
- The Company received a \$25 million YUPELRI[®] U.S. sales milestone from Viatris in January 2026 and a \$50 million TRELEGY milestone from Royalty Pharma in February 2026.
- After receiving the TRELEGY and YUPELRI[®] milestones in Q1 2026, the Company expects to have approximately \$400 million in cash at the end of Q1 2026.
- The Company also benefits from approximately \$2.6 billion of Irish tax attributes.

About Amprexetine

Amprexetine, an investigational, once-daily norepinephrine reuptake inhibitor in development for the treatment of symptomatic neurogenic orthostatic hypotension (nOH) in patients with multiple system atrophy (MSA).

About CYPRESS (Study 0197), a Phase 3 Study

Study 0197 ([NCT05696717](https://clinicaltrials.gov/ct2/show/study/NCT05696717)) is a registrational Phase 3, multi-center, randomized withdrawal study to evaluate the efficacy and durability of amprexetine in participants with MSA and symptomatic nOH after 20 weeks of treatment; the primary endpoint of the study is change in the Orthostatic Hypotension Symptom Assessment (OHSA) composite score. Secondary endpoints include change from baseline in Orthostatic Hypotension Daily Activity Scale (OHDAS) composite score, OHDAS item 1 (activities that require standing for a short time) and OHDAS item 3 (activities that require walking for a short time).

About Theravance Biopharma

Theravance Biopharma, Inc.'s focus is to deliver *Medicines that Make a Difference*[®] in people's lives. In pursuit of its purpose, Theravance Biopharma leverages decades of expertise, which has led to the development of FDA-approved YUPELRI[®] (revefenacin) inhalation solution indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). The Company is committed to creating/driving shareholder value.

For more information, please visit www.theravance.com.

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YUPELRI® is a registered trademark of Mylan Specialty L.P., a Viatris company. Trademarks, trade names or service marks of other companies appearing in this press release are the property of their respective owners.

Preliminary Financial and Operating Results

The financial information in this press release is preliminary, unaudited, based on currently available information, and subject to adjustment in the final financial statements to be filed with the Company's Annual Report on Form 10-K for the year ended December 31, 2025. The preliminary results set forth above reflect preliminary, unaudited estimates based solely on currently available information, which is subject to change. Such preliminary results are subject to the finalization of year-end financial and accounting procedures. While carrying out such procedures, the Company may identify items that would require it to make adjustments to the preliminary estimates of financial results set forth herein. As a result, the Company's actual financial results could differ from the information set forth herein and such differences could be material. Moreover, preliminary and estimated financial results should not be viewed as a substitute for the Company's full annual financial statements for the year ended December 31, 2025, which will be prepared in accordance with U.S. GAAP.

Forward-Looking Statements

This press release contains certain "forward-looking" statements as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, statements relating to goals, plans, objectives, expectations and future events. Theravance Biopharma intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995. Examples of such statements include statements relating to: the Company's expectations regarding its future profitability, expenses and uses of cash, the Company's goals, designs, strategies, plans and objectives, future growth of YUPELRI sales and future royalty payments, the winddown of the Company's ampreloxadine program and R&D function and significant reduction of its G&A function, the consideration of strategic alternatives for the Company, the ability to provide value to shareholders, the Company's regulatory strategies, data regarding our investigational therapy, the status of patent infringement litigation initiated by the Company and its partner against certain generic companies in federal district courts, and contingent milestone payments due to the Company from the sale of the Company's TRELEGY royalty interests. These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of this press release and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance Biopharma to be materially different from those reflected in the forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, risks related to: factors that could increase the Company's expenses beyond its expectations and any factors that could adversely affect its profitability, whether the TRELEGY milestone thresholds will be achieved, delays or difficulties in winding down clinical studies, the potential that results from analysis of clinical or non-clinical studies indicate the Company's product candidates or product are unsafe, ineffective or not differentiated, risks of decisions from regulatory authorities that are unfavorable to the Company, delays or failure to achieve and maintain regulatory approvals for product candidates, the timing of any potential strategic transaction with respect to the Company, if at all, risks of collaborating with or relying on third parties to discover, develop, manufacture and commercialize products, and risks associated with establishing and maintaining sales, marketing and distribution capabilities with appropriate

technical expertise and supporting infrastructure, the ability of the Company to protect and to enforce its intellectual property rights, volatility and fluctuations in the trading price and volume of the Company's shares, and general economic and market conditions. Other risks affecting Theravance Biopharma are in the Company's Form 10-Q filed with the SEC on November 12, 2025, and other periodic reports filed with the SEC. In addition to the risks described above and in Theravance Biopharma's filings with the SEC, other unknown or unpredictable factors also could affect Theravance Biopharma's results. No forward-looking statements can be guaranteed, and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Theravance Biopharma assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law.

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