



Corporate Presentation

December 10, 2024



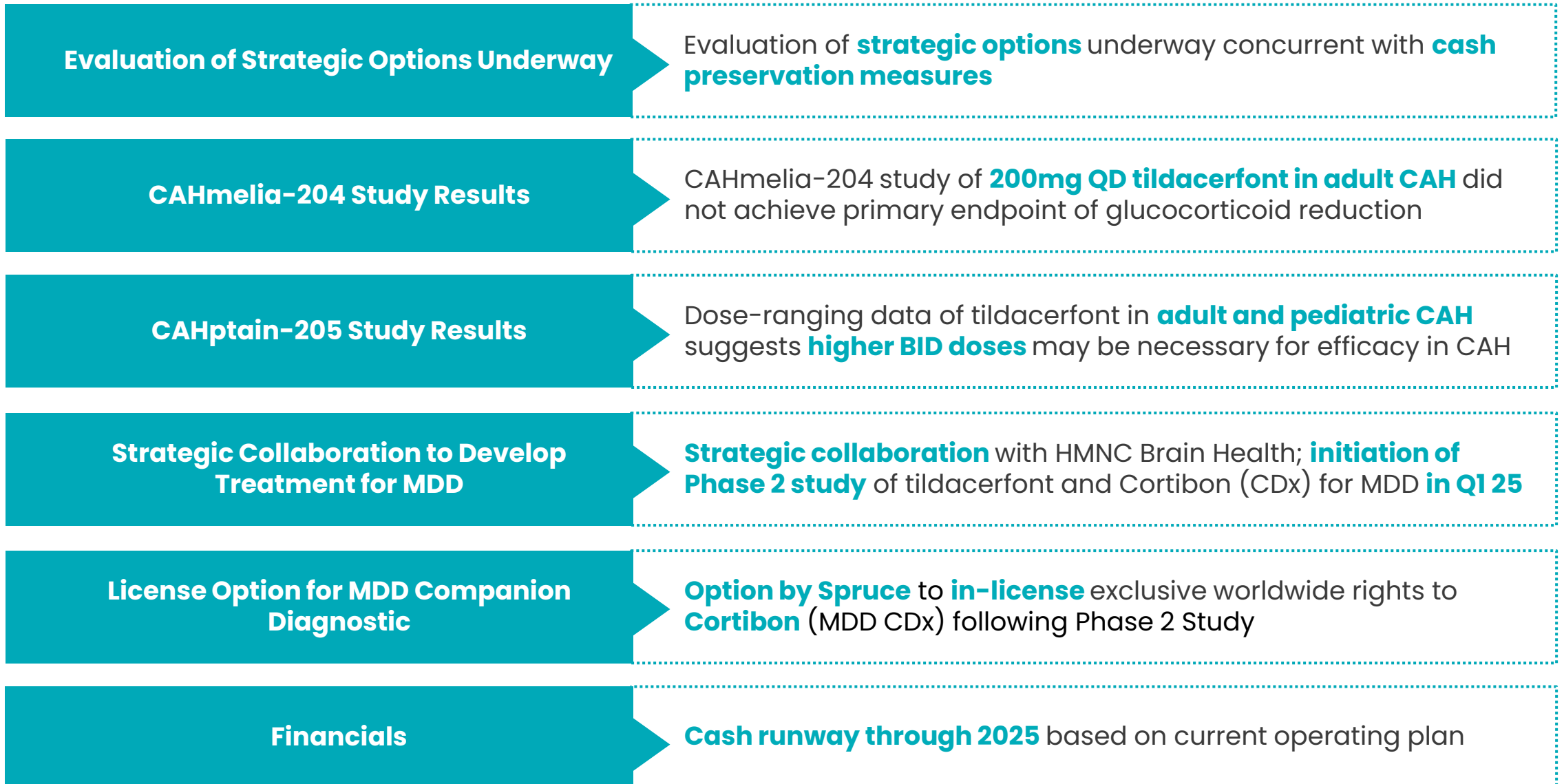
Forward Looking Statements

This presentation contains forward-looking statements about Spruce Biosciences, Inc. (“we,” “Spruce” or the “Company”). All statements other than statements of historical facts contained in this presentation are forward-looking statements, including statements about our strategy, our expectations regarding the timing and achievement of our product candidate’s development activities and ongoing and planned clinical trials, and plans and expectations for future operations. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to: our limited operating history; net losses; our expectation that we will incur net losses for the foreseeable future, and that we may never be profitable; our need for additional funding and related risks for our business, product development programs and future commercialization activities; the timing and success of clinical trials we conduct; the ability to obtain and maintain regulatory approval of our product candidate; the ability to commercialize our product candidate; our ability to compete in the marketplace; risks regarding our license agreement; our ability to obtain and maintain intellectual property protection for our product candidate; and our ability to manage our growth. We operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations.

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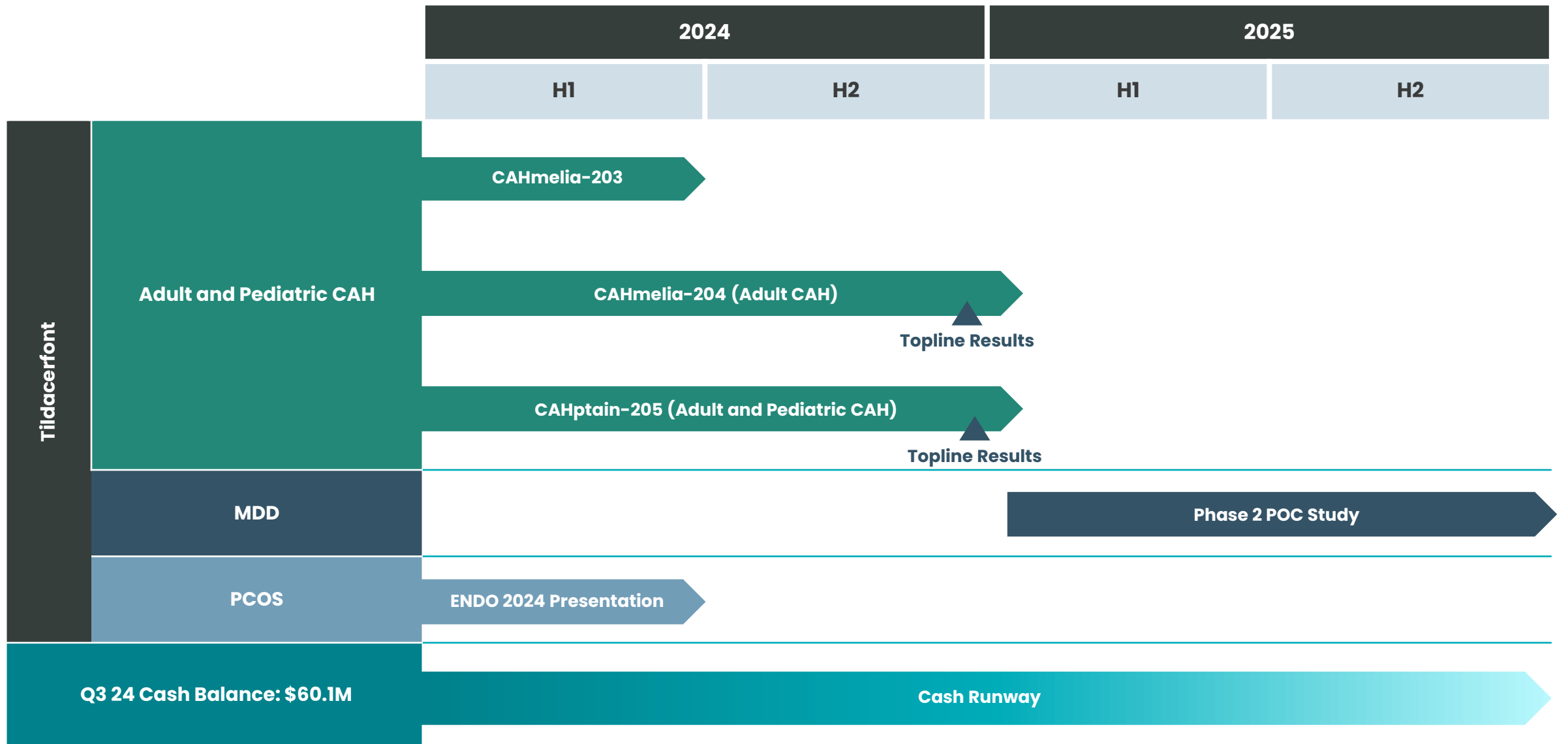
This presentation discusses a product candidate that is under clinical study and which has not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of this product candidate for the use for which it is being studied.

Spruce Bio At a Glance



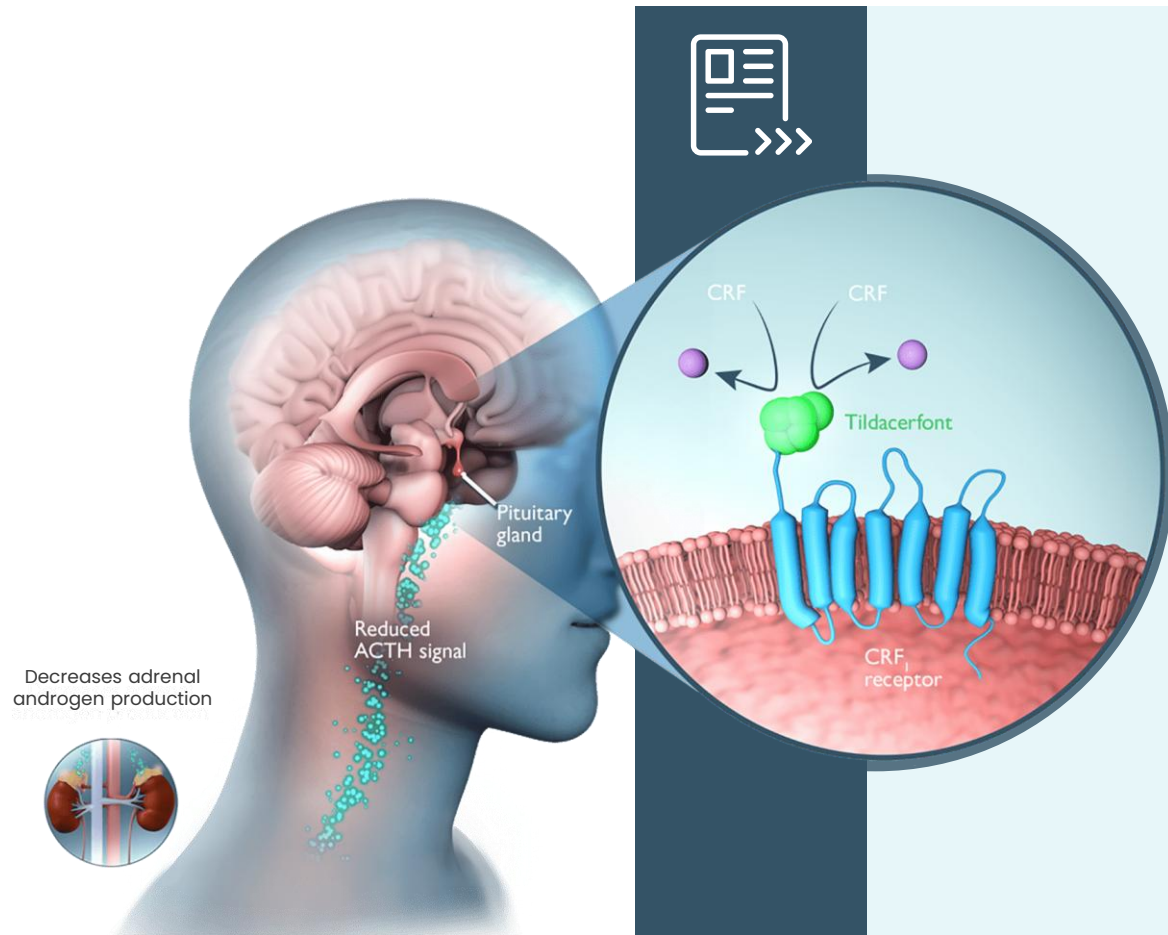
Note: CAH is congenital adrenal hyperplasia, MDD is major depressive disorder; PCOS is polycystic ovary syndrome, CDx is companion diagnostic.

Overview of Anticipated Milestones and Cash Runway



Note: CAH is congenital adrenal hyperplasia, MDD is major depressive disorder; PCOS is polycystic ovary syndrome.

Tildacerfont is a Second-Generation CRF₁ Receptor Antagonist



Tildacerfont is an oral, second generation CRF₁ receptor antagonist¹



Tildacerfont binds to CRF₁ receptors in the pituitary gland, blocking receptor stimulation by the hypothalamus¹


ACTH, adrenocorticotropic hormone; CRF, corticotropin-releasing factor; CRF₁, corticotropin-releasing factor 1.

1. Sarafoglou K, et al. *J Clin Endocrinol Metab.* 2021:dgab438. DOI: <https://doi.org/10.1210/clinem/dgab438> [Epub ahead of print].

Treatment Options in MDD Demonstrate Suboptimal Efficacy

MDD biology and pathogenesis¹

Genetic environmental psychological and biological factors cause MDD




- I. HPA axis dysfunction hypothesis
- II. Monoamine hypothesis
- III. Inflammatory hypothesis
- IV. Genetic and Epigenetic anomaly hypothesis
- V. Structural and functional brain remodeling hypothesis
- VI. Social psychological hypothesis

HMNC focus

Pharmacotherapy is one of complementary treatment options, but shows suboptimal efficacy

Pharmacotherapy

Antidepressants cover a broad spectrum of **mechanisms of action**...



- ✓ Selective serotonin reuptake inhibitors
- ✓ Serotonin noradrenalin reuptake inhibitors
- ✓ Noradrenalin and dopamine reuptake inhibitors
- ✓ Noradrenalin and specific serotonergic antidepressants
- ✓ Melatonergic agonist
- ✓ Tricyclic antidepressants
- ✓ Second generation antipsychotics
- ✓ Monoamine oxidase inhibitors
- ✓ NMDA receptor modulator


+

Psychotherapy


Brain stimulation

Lifestyle change


...but out of **100** patients...



...**72** fail to achieve remission after first line of antidepressant treatment...

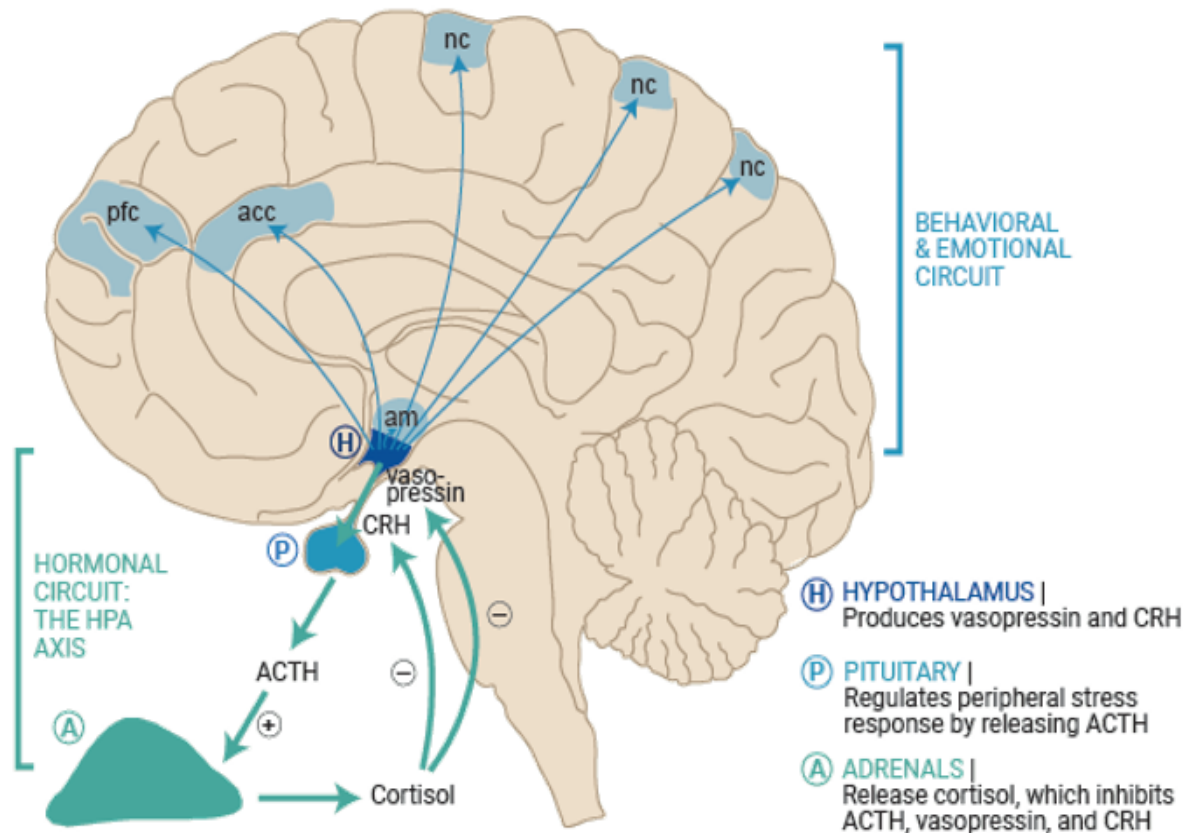


...and **34** fail to remit even after multiple lines of treatment²



¹Cui, Lulu, et al. (2024) ²Rush et al (2009)

Substantial Subset of MDD Patients Possess HPA-Axis Disturbance



Background

- A substantial subset (~30-50%) of all patients with MDD have a disturbance in CRH signaling, key stress response regulators

Breakthrough

- Cortibon has the potential to identify especially those patients, with high specificity and sensitivity
- Tildacerfont has the potential to be highly efficacious in CDx-positive patients

CRHR1 Antagonists – Why were they shelved?

- Developmental programs that target the HPA axis were conducted in non-selected patient populations and therefore, did not show significant efficacy

"We reviewed a range of issues that may explain why CRHR1 antagonists have been challenging to translate from bench to bedside. These include potential specificity limitations of preclinical models and the fact that CRHR1 antagonists produced therapeutic-like results only under specific conditions, unlike some clinically effective compounds that act more generally." Reference: [Spierling, Zorrilla \(2017\)](#)

Financial Highlights

Capital Structure and Summary Financials as of September 30, 2024

Capital Structure	Shares (M)
Shares Outstanding	41.3
Equity Awards Issued and Outstanding	7.9
Common Stock Warrants	12.7
Fully Diluted Shares Outstanding	61.9

Financials	000's
Cash & Cash Equivalents	\$60,055
Debt ¹	\$2,163

1. Term loan, gross balance as of September 30, 2024.



spruceBIOSCIENCES

