SPN-820 Phase 2a Study

Exploratory Open-Label Study in Adults with Major Depressive Disorder

October 17, 2024

Safe Harbor Statement

This presentation and other matters discussed today or answers that may be given to questions asked include forward-looking statements within the meaning of the federal securities laws. These statements, among other things, relate to Supernus' business strategy, goals and expectations concerning its products and product candidates including SPN-820, future operations, prospects, plans and objectives of management. The words "anticipate", "believe", "could", "estimate", "expect", "intend", "may", "plan", "predict", "project", "will", and similar terms and phrases are used to identify forward-looking statements in this presentation. Supernus' operations involve risks and uncertainties including the risk factors set forth from time to time in Supernus' filings with the U.S. Securities and Exchange Commission (SEC), which could materially affect its results of operations and whether the forward-looking statements ultimately prove to be correct. Supernus assumes no obligation to update any forward-looking statements except as required by applicable law.

Supernus has filed with the SEC reports and other documents required by Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended. Before you purchase any Supernus securities, you should read such reports and other documents to obtain more complete information about the company's operations and business and the risks and uncertainties that it faces in implementing its business plan. You may get these documents for free by visiting EDGAR on the SEC website at http://www.sec.gov.

Participants

Jack Khattar
President and Chief Executive Officer

Jonathan Rubin, M.D., MBA
SVP, Research and Development, Chief Medical Officer

Introduction and Agenda

- Executive Summary
- SPN-820 Overview
- Phase 2a Open-Label Study Design and Results
- Summary & Conclusions

Executive Summary

- SPN-820 restores mTORC1 synaptic signaling through a first in class, unique intracellular mechanism
- Completed a Phase 2a exploratory open-label study in adults with major depressive disorder (MDD)
  - Rapid decrease in depression symptoms, beginning within hours of first dose
  - Substantial effect on depression symptoms observed in two depression scales
  - Substantial reduction in suicidal ideation
  - Well-tolerated with few adverse events (AEs) and low discontinuation rate

SPN-820 Description

- SPN-820 is an oral product candidate for the treatment of depression
- Novel, first in class, intracellular modulator of mTORC1
- Demonstrated to increase brain derived neurotrophic factor (BDNF) and other downstream modulators in animal models
- Increased dendritic spines in animal model supporting neuroplasticity
- Prior proof of concept Phase 1b study demonstrated significantly improved depressive symptoms 4 hours after a single dose

Phase 2a Study Objectives

- Subjects with MDD
- Assess rapid onset of improvement in depression symptoms
- Evaluate once every 3-day dosing
- Assess safety and tolerability

Phase 2a Open-Label Adjunctive Design

- Open-label, single group, 2400 mg single dose on Days 1, 4, and 7
- Adults (aged 18 to 65 years) with MDD
  - Montgomery-Åsberg Depression Rating Scale (MADRS) total score ≥22 at screening and baseline
  - Clinical Global Impression-Severity of Illness (CGI-S) ≥4 (moderately ill or worse) at screening and baseline
  - Maintained on a stable, approved dose of antidepressant therapy (ADT) for current major depressive episode ≥6 weeks and remained on the ADT during the study
- N=40

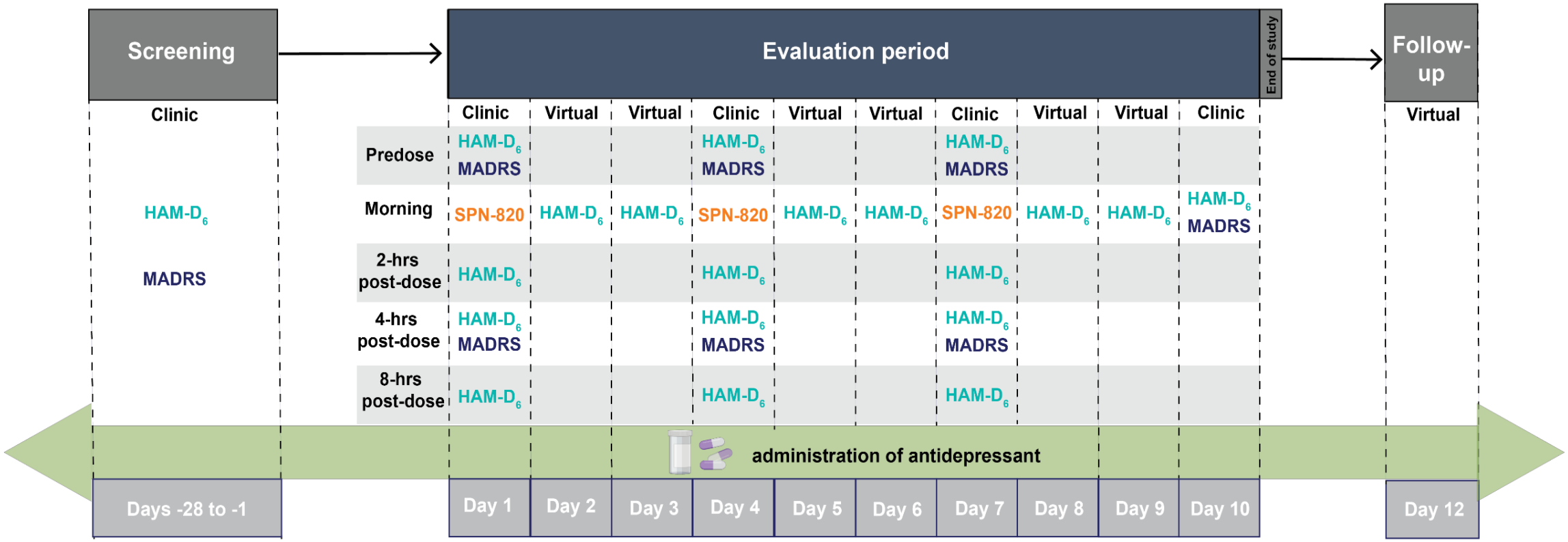
Efficacy Endpoints

- Primary endpoint (at each timepoint):
  - Change from Baseline (CFB) in the Hamilton Depression Rating Scale-6 Items (HAM-D_6) total score
- Secondary efficacy endpoint (at each timepoint):
  - CFB in the MADRS total score

Safety Endpoints

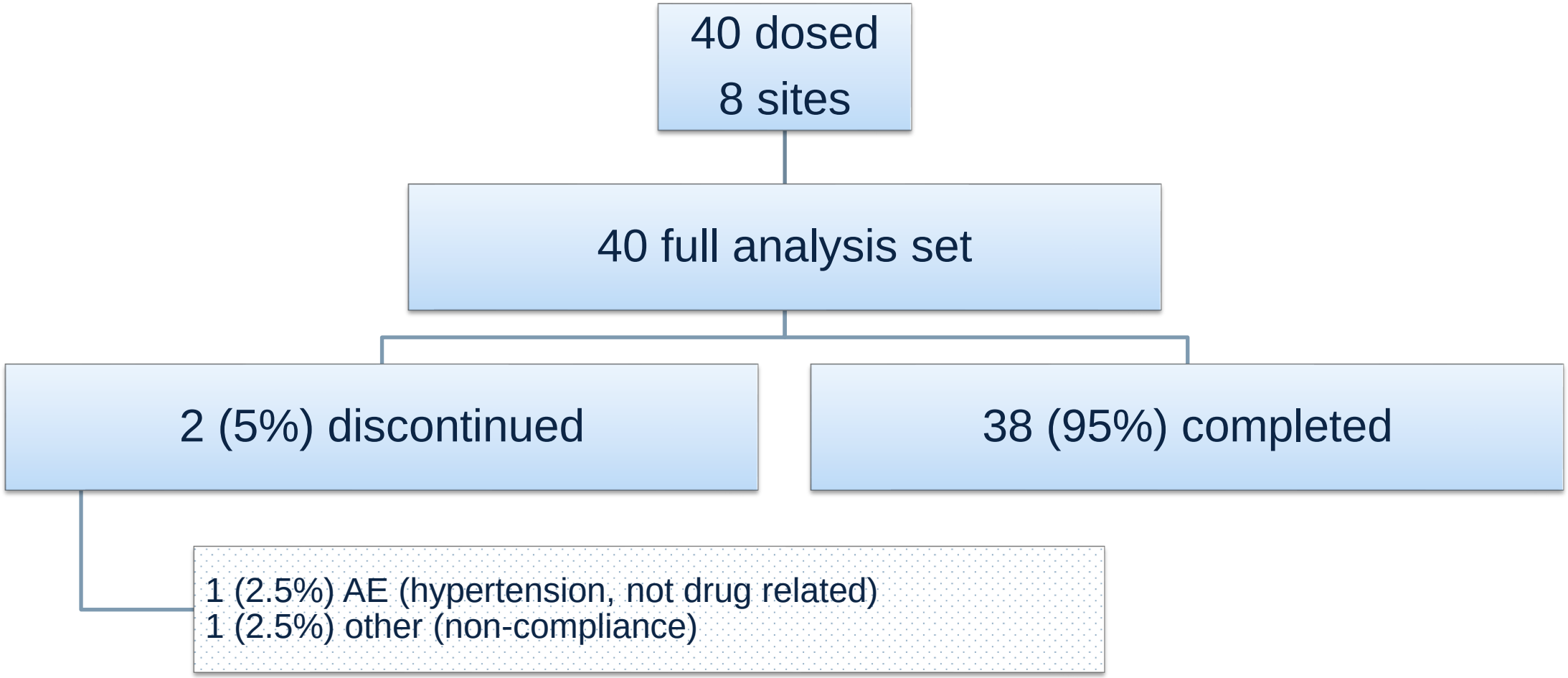
- Adverse Events (AEs)
- Suicidal ideation and behaviors measured by the Columbia Suicide Severity Rating Scale (C-SSRS) score
- Clinician Administered Dissociative State Scale (CADSS) score
- Brief Psychiatric Rating Scale Positive Total Score (BPRS+) score

Phase 2a Open-Label Study Schematic



Supernus® Pharmaceuticals

Subject Disposition



Subject Demographics

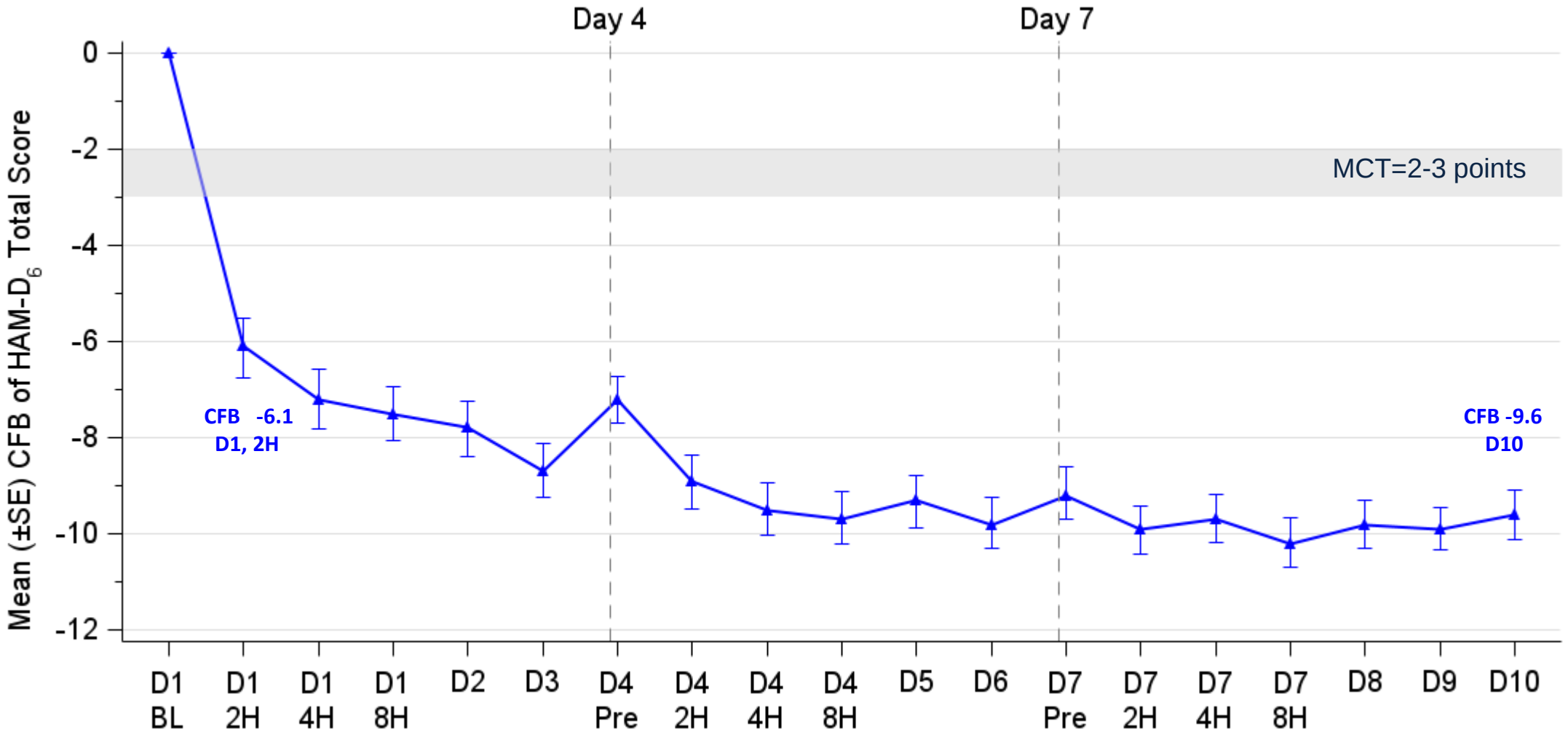
Parameter	Mean ± Standard Deviation (Min, Max) or (%) N=40
Age (years)	44.7 ± 15.39 (18, 64)
Sex	• Female (67.5%) • Male (32.5%)
Race	• White (80.0%) • Black (7.5%) • Asian (10.0%) • Unknown (2.5%)
Weight (kg)	81.8 ± 19.92 (48.4, 126.9)
BMI (kg/m^2)	28.6 ± 5.43 (19.4, 39.5)

Baseline Characteristics

Severity Assessment	Mean ± Standard Deviation (Min, Max)
HAM-D_6 Total Score	13.6 ± 1.69 (9, 17)
MADRS Total Score	33.1 ± 5.41 (22, 42)
CGI-S Score	4.6 ± 0.64 (4, 6)

HAM-D_6 score of 13-22 is severe, 9-12 is moderate
MADRS score of 34-60 is severe, 20-33 is moderate
CGI-S score of 4 is moderate, 5 is marked

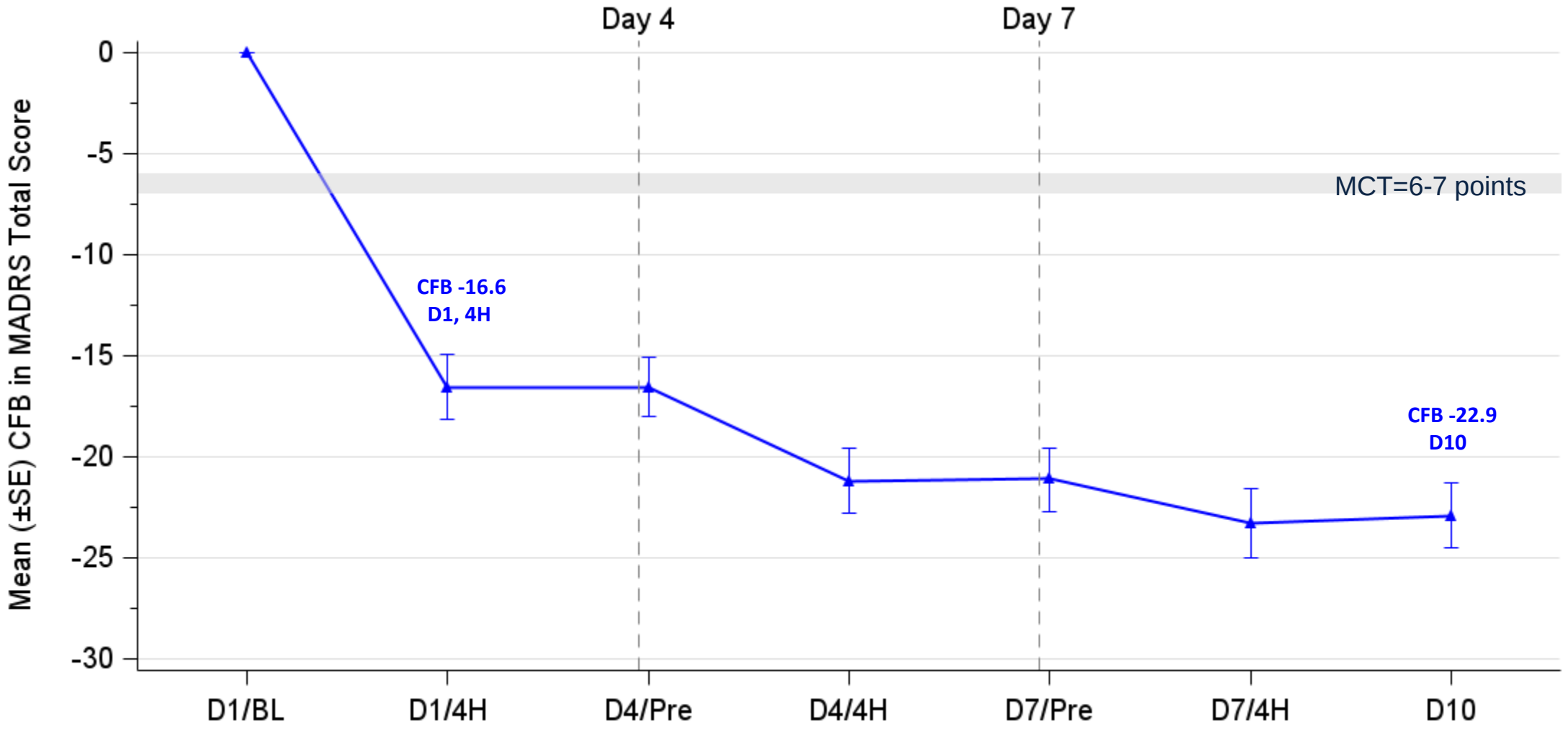
Rapid Decrease in HAM-D_6 Scores



D: Day; BL: Baseline; H: Hour; Pre: Pre-dose; SE: Standard Error; CFB: Change from Baseline; MCT: Meaningful Clinical Threshold.

Supernus® Pharmaceuticals

Rapid Decrease in MADRS Scores



D: Day; BL: Baseline; H: Hour; Pre: Pre-dose; SE: Standard Error; CFB: Change from Baseline; MCT: Meaningful Clinical Threshold.

Supernus® Pharmaceuticals

Summary of Treatment-Emergent Adverse Events (TEAEs)

Category	Subjects (N=40) n (%)
TEAE	25 (62.5%)
Related TEAE	23 (57.5%)
Serious Adverse Event (SAE)	0
Severe TEAE	0
TEAE Leading to Withdrawal	1 (2.5%)*

*Increase in severity of hypertension on Day 4 which was assessed by the principal investigator as moderate in severity and not related to the study medication.

Supernus® Pharmaceuticals

Well-Tolerated with Few AEs

Adverse Event	Subjects (N=40)
Headache	8 (20.0%)
Nausea	8 (20.0%)
Somnolence	6 (15.0%)
Dizziness	4 (10.0%)
Cognitive disorder	2 (5.0%)
Dry mouth	2 (5.0%)
Fatigue	2 (5.0%)
Nasal congestion	2 (5.0%)
Paresthesia oral	2 (5.0%)

- CADSS and BPRS+ assessments showed no changes regarding dissociative events or psychosis

Substantial Decrease in Suicidal Ideation

- Suicidal ideation decreased by 80%
  - 5/40 (12.5%) with suicidal ideation at baseline
  - 1/38 (2.6%) with suicidal ideation at Day 10
- No suicidal behavior during the study

Rapid Acting, Highly Tolerable, First in Class Antidepressant

- Rapid and substantial decrease (as early as 2 hours) in depressive symptoms
  - Clinically meaningful change in both HAM-D_6 and MADRS
- Single dose lasting 72 hours
- 80% decrease in suicidal ideation
- Well-tolerated with few AEs
  - Low discontinuation rate of 2.5% due to AEs

SPN-820 Phase 2b Enrollment Update

- Double-blind placebo controlled adjunctive study of subjects with treatment-resistant depression (TRD)
- 227 randomized (target 236)
- Primary endpoint: MADRS total score
- Enrollment expected to complete November 2024
- Topline data expected 1H 2025