ALKS 5461: FORWARD-3 and FORWARD-4

American Society of Clinical Psychopharmacology Annual Meeting

JUNE 1, 2016

Forward-Looking Statements

Certain statements in this presentation may constitute “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning future business plans or prospects of Alkermes plc; the timing, funding and feasibility of product development activities for ALKS 5461; whether the studies conducted for our development programs, including ALKS 5461, will meet FDA’s requirements; and the therapeutic value and commercial potential of ALKS 5461 and our other products. Although the company believes that such forward-looking statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those expressed or implied in the forward-looking statements due to risks and uncertainties. The factors that could cause actual results to differ are described under the heading “Risk Factors” in the Alkermes plc Annual Report on Form 10-K for the fiscal year ended Dec. 31, 2015, and in other subsequent filings made by the company with the U.S. Securities and Exchange Commission (SEC), which are available on the SEC's website at www.sec.gov and on the company’s website at www.alkermes.com in the “Investors—SEC filings” section. The information contained in this presentation is provided by the company as of the date hereof and, except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking information contained herein.

ALKS 5461 in Major Depressive Disorder: Results From FORWARD Pivotal Program Being Presented at ASCP

Elliot Ehrich, M.D., Chief Medical Officer

ALKS 5461 in Major Depressive Disorder (MDD)

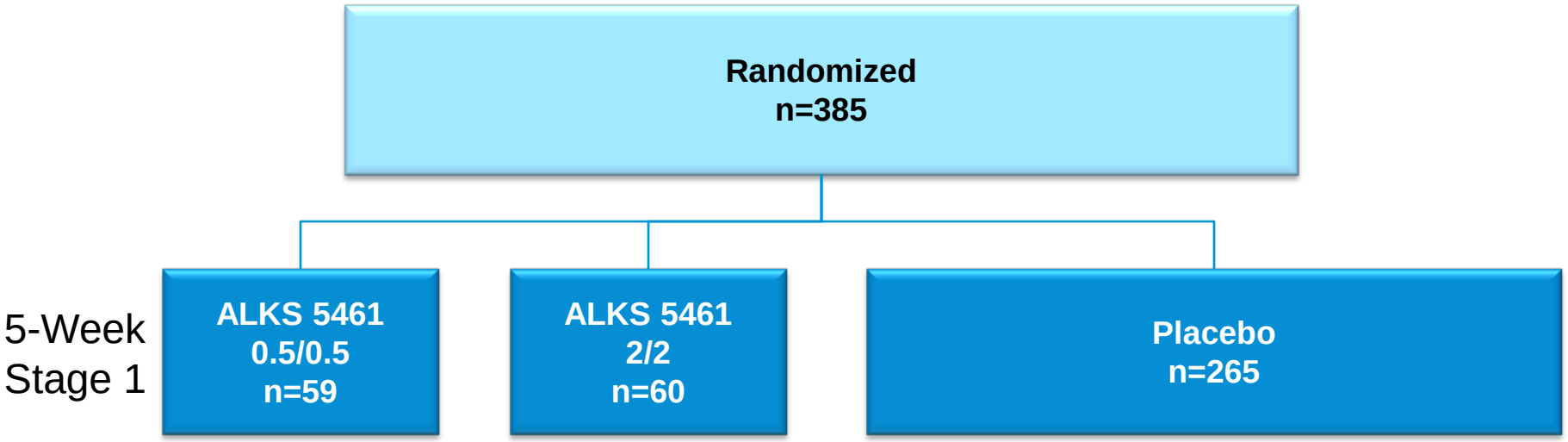
1. Centrally-acting opioid modulator with novel mechanism of action, addressing dysregulation of endogenous endorphin and dynorphin neuropeptides
2. Comprised of buprenorphine (partial opioid agonist) co-formulated with NME samidorphan (opioid antagonist) designed to normalize neurotransmission without addictive properties of classic opioids
3. Evidence from positive phase 2 clinical studies supporting anti-depressive effects and Fast Track status
4. 50% of placebo-controlled studies of FDA-approved MDD medicines failed[1]; Sequential Parallel Comparison Design (SPCD) studies are designed to address placebo response

[1] Iovieno N. and Papakostas G. *J Clin Psych*. 2012; 73(10):1300-6

FORWARD Efficacy Studies Focus on Important Patient Population

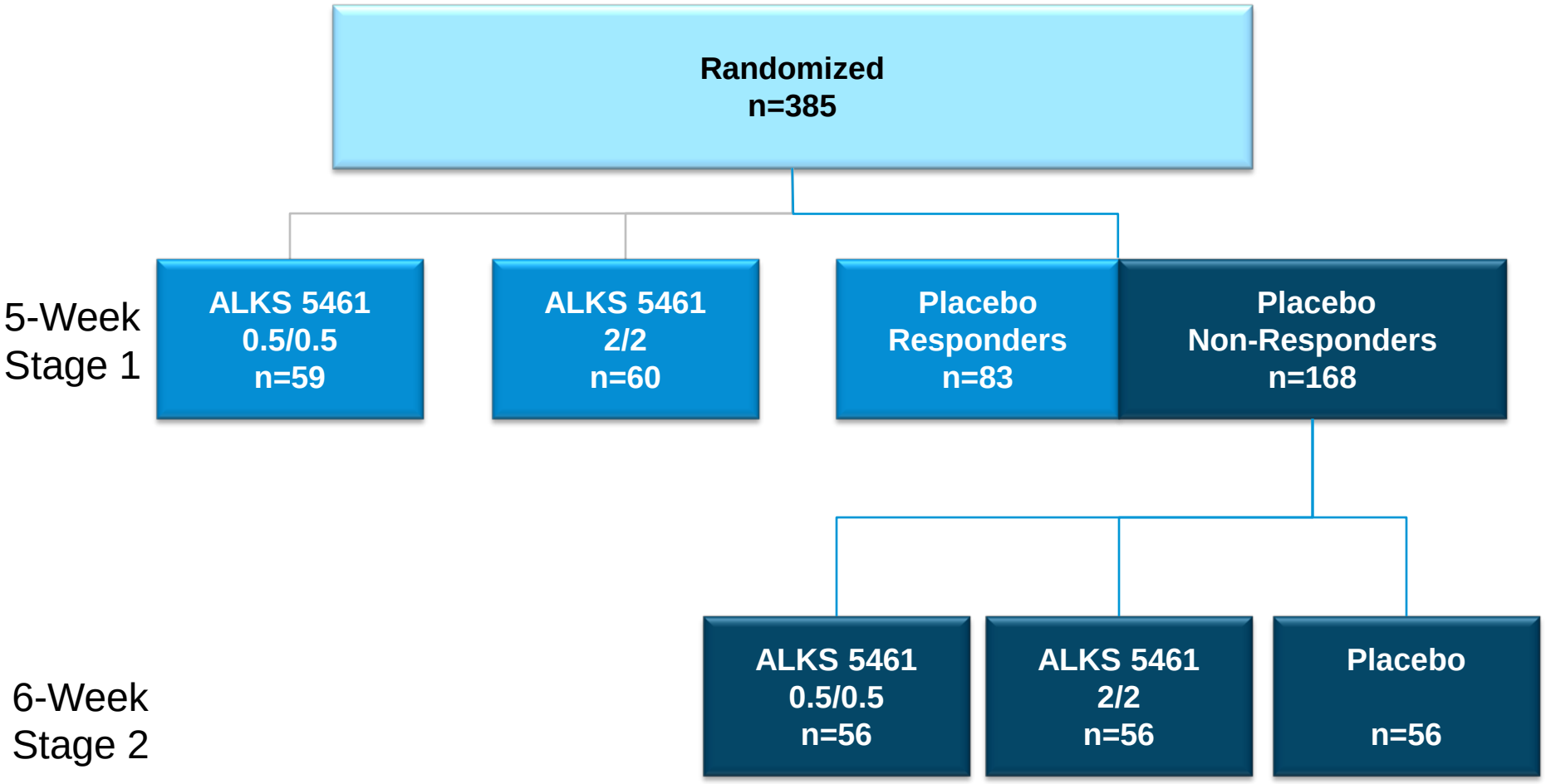
- Confirmed diagnosis of Major Depressive Disorder
- Inadequate response to standard antidepressant treatment
  - Hamilton Depression Rating Scale (HAM-D) score ≥ 18, despite adequate trial of SSRI or SNRI
- Adjunctive therapy
  - Subjects remain on background antidepressant therapy
  - Randomized to receive ALKS 5461 or matching placebo

FORWARD-4: SPCD Stage 1 Subject Flow



Following randomization, one subject did not receive study drug and is excluded from the safety and efficacy analysis

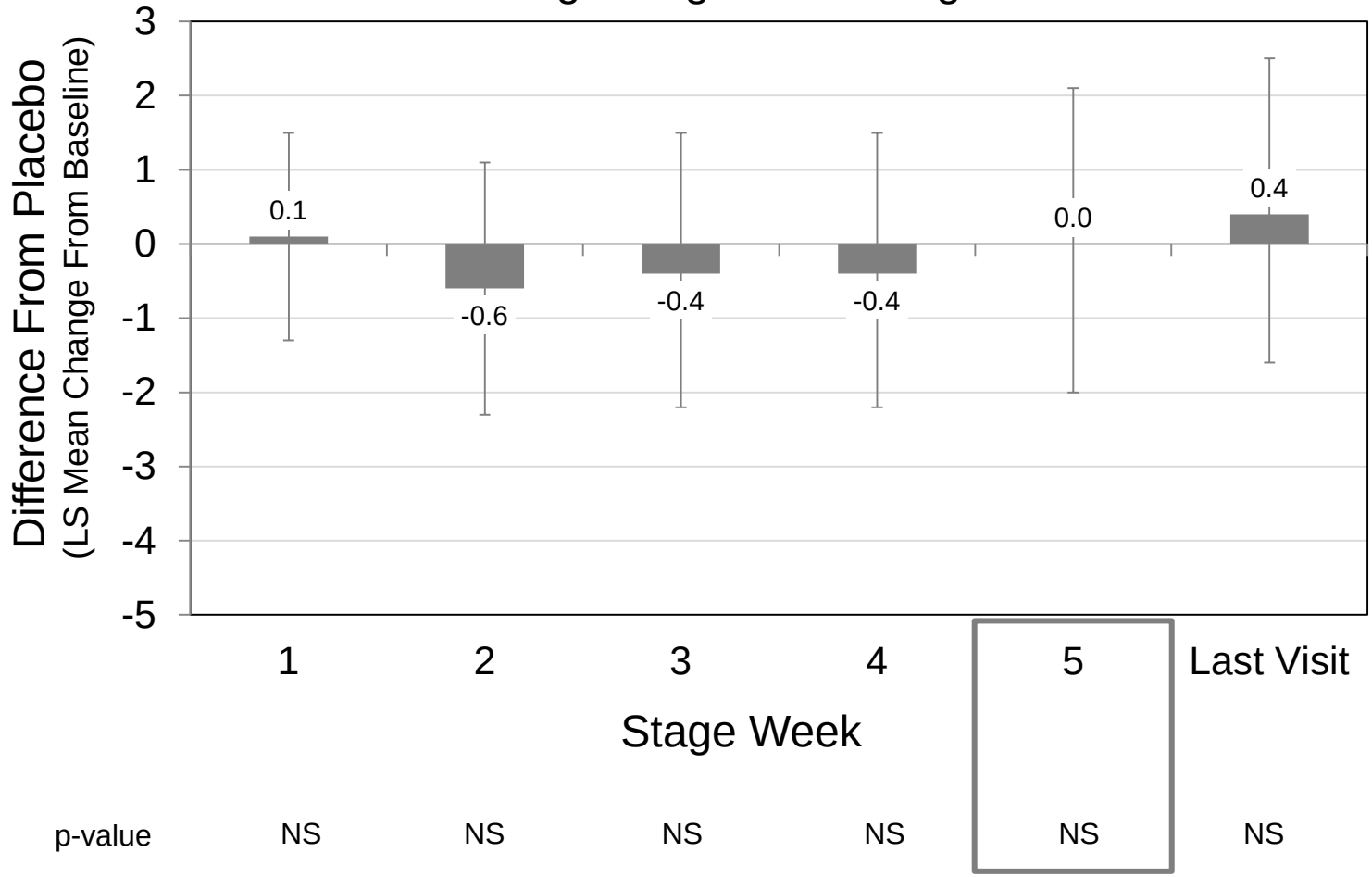
FORWARD-4: SPCD Stage 2 Subject Flow



14 subjects in the Stage 1 placebo group did not complete Stage 1. All efficacy analyses include subjects that received ≥ 1 dose of study drug and had ≥ 1 post-baseline Montgomery-Åsberg Depression Rating Scale (MADRS) assessment.

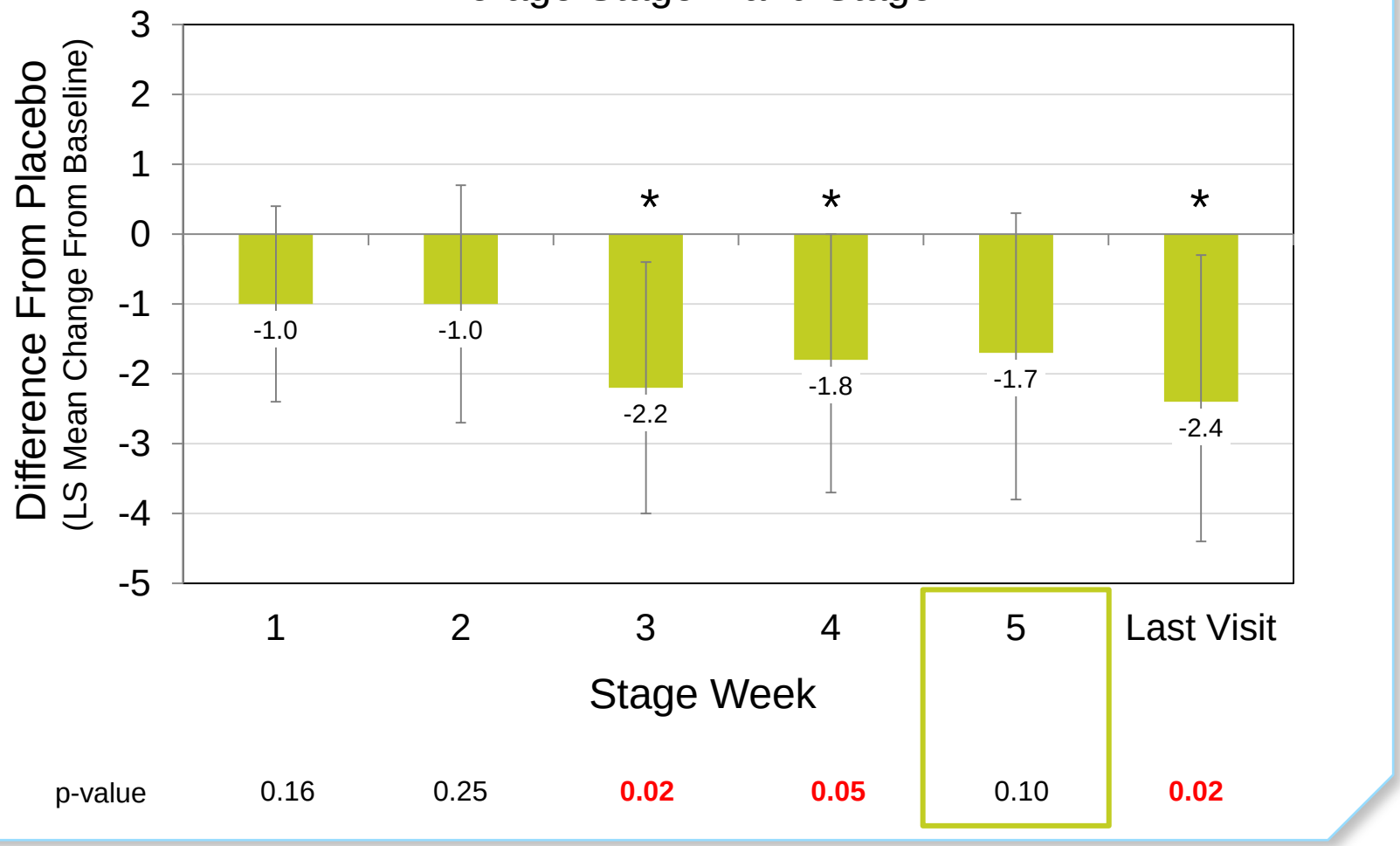
Alkermes

ALKS 5461 FORWARD-4 Primary Analysis: 0.5/0.5 Dose vs. Placebo by Stage Week



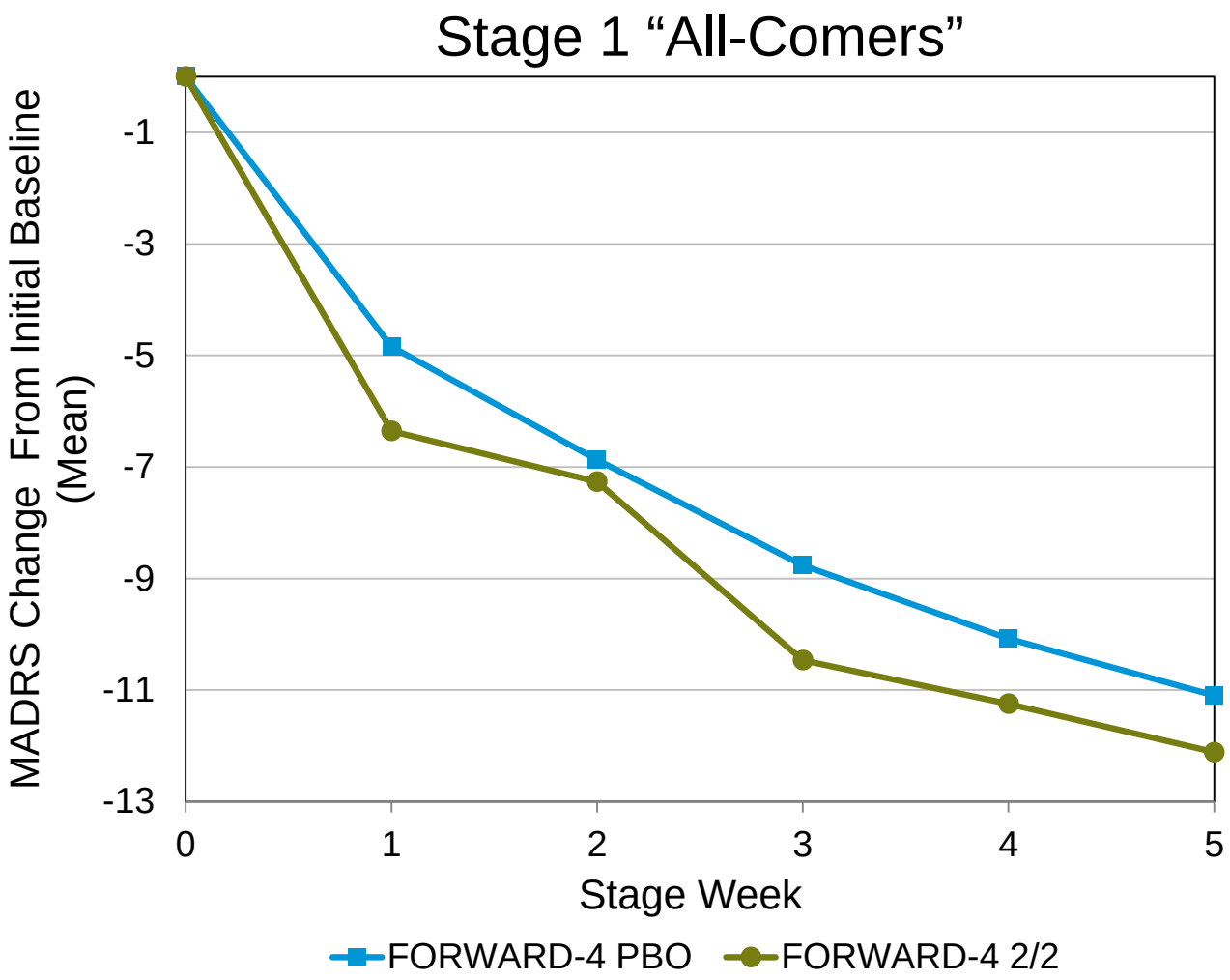
95% confidence interval

ALKS 5461 FORWARD-4 Primary Analysis: 2/2 Dose vs. Placebo by Stage Week

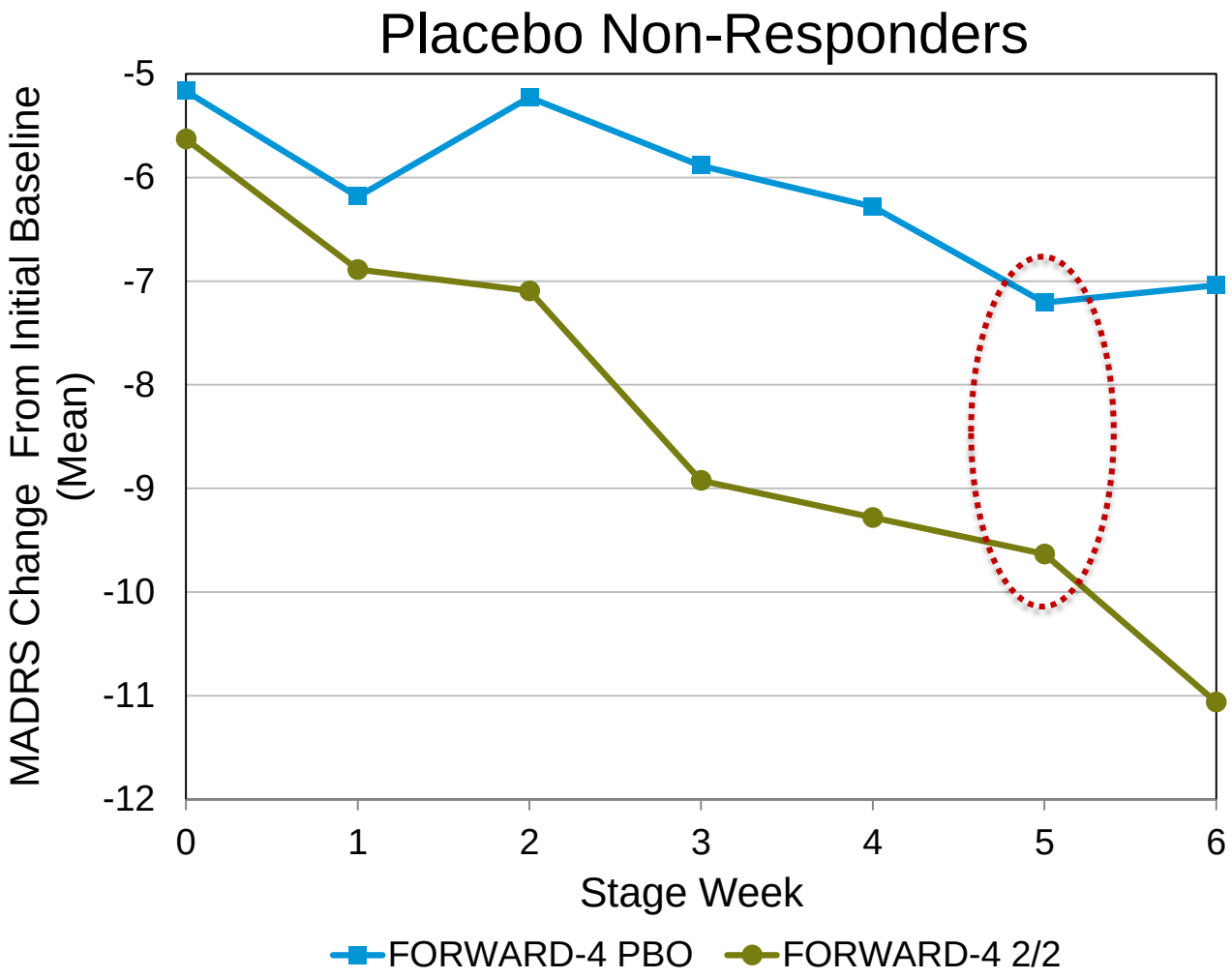


95% confidence interval

ALKS 5461 FORWARD-4 Stage 1: 2/2 Dose, MADRS Change From Baseline by Stage Week



ALKS 5461 FORWARD-4 Stage 2: 2/2 Dose, MADRS Change from Baseline by Stage Week



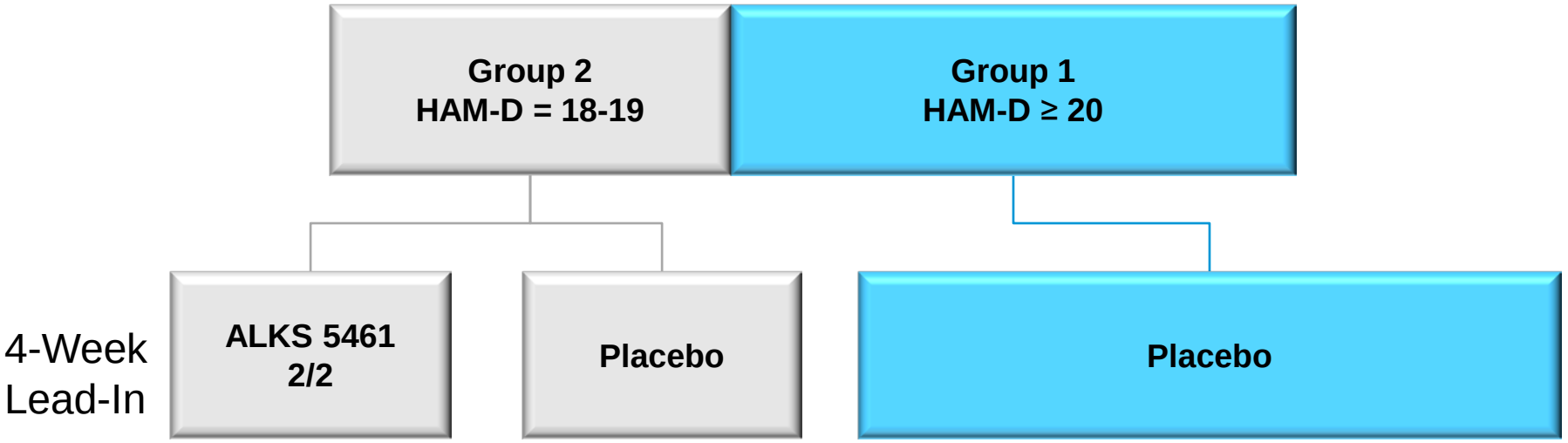
Subjects meeting placebo non-responder criteria at end of Stage 1 were re-randomized in Stage 2

Alkermes

FORWARD-4 Summary

- Sequential Parallel Comparison Design (SPCD) performed as expected
- Clear evidence of efficacy
  - Primary analysis was not statistically significant at pre-specified Week 5 time point
  - Significant at other time points and over full study period

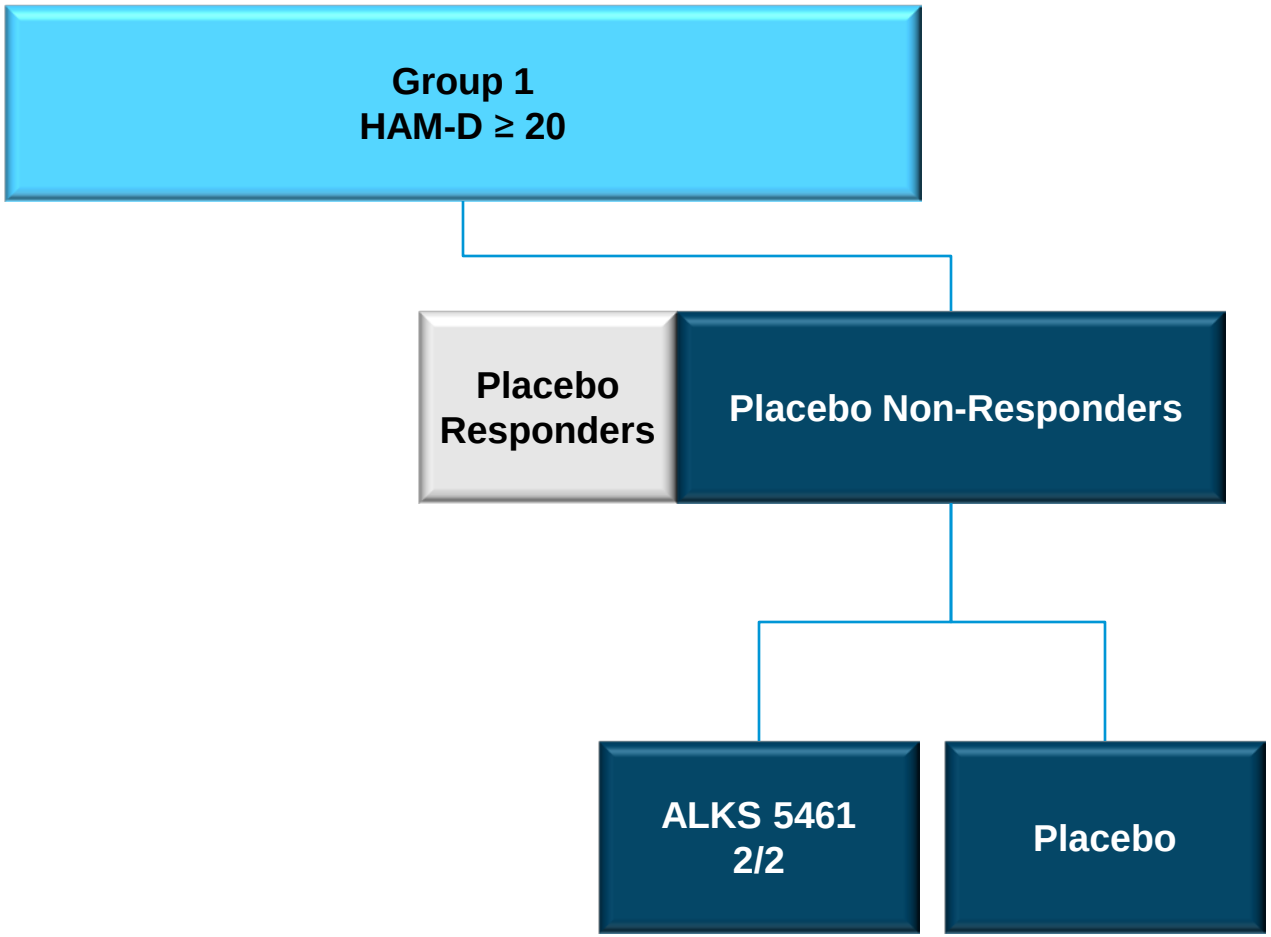
FORWARD-3 Design: HAM-D ≥ 20, Placebo Lead-in



FORWARD-3: Efficacy Analysis

4-Week Lead-In

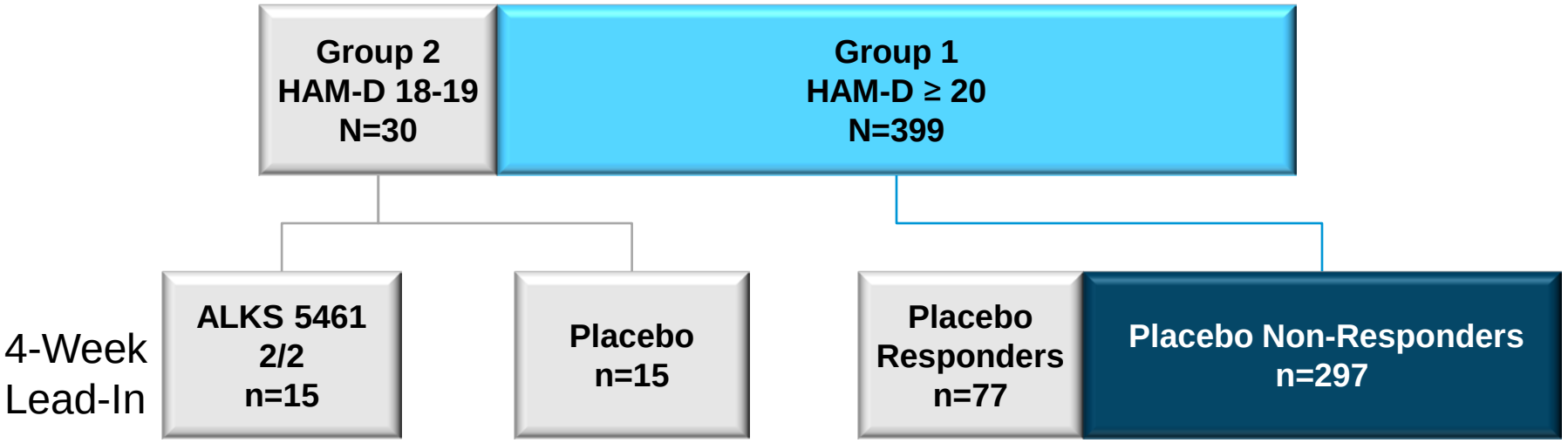
6-Week Efficacy Phase



All efficacy analyses include placebo non-responders from the 4-week lead-in who received ≥ 1 dose of study drug and had ≥ 1 post-baseline MADRS assessment during the efficacy phase

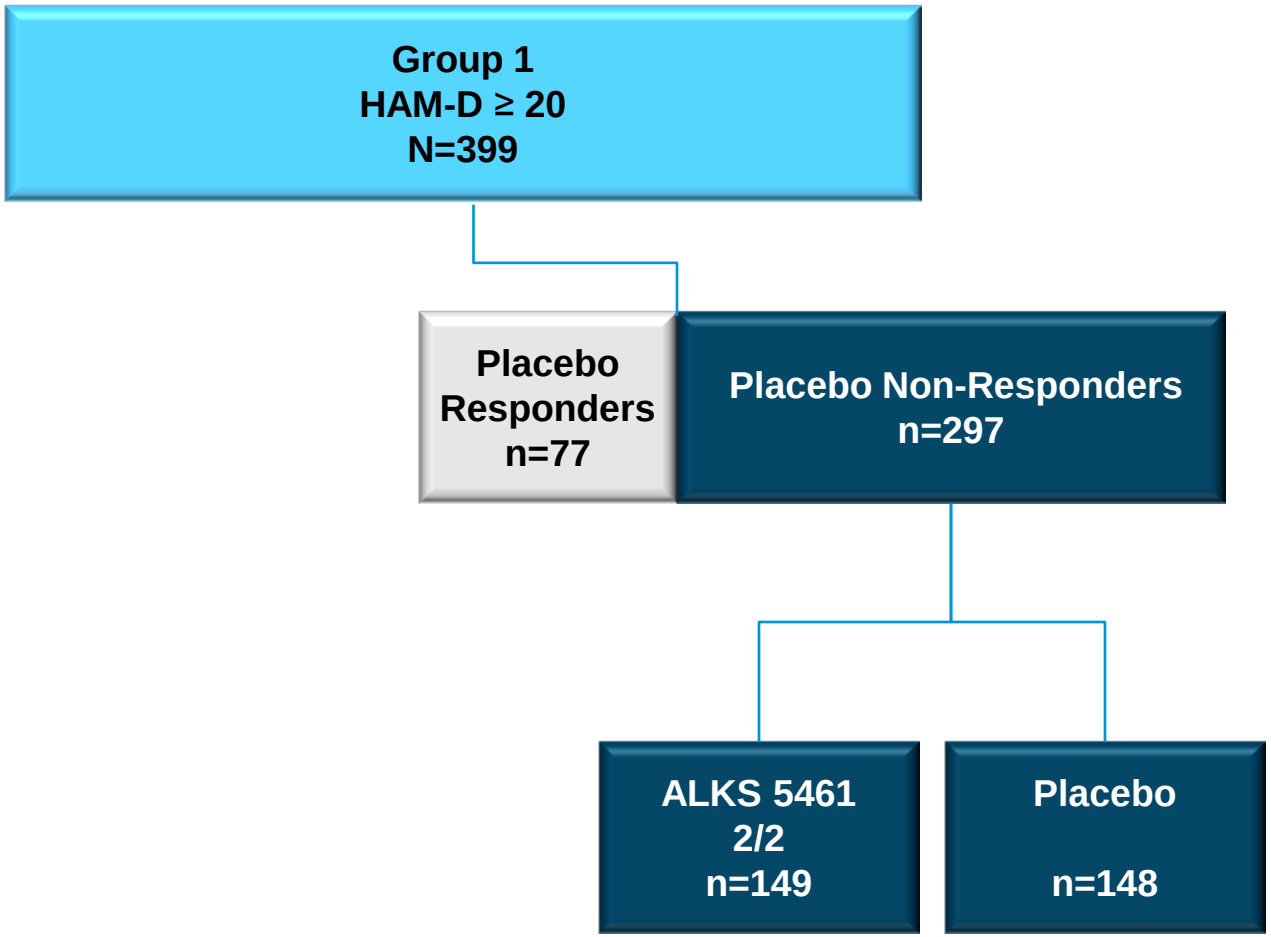
Alkermes

FORWARD-3: Subject Flow



25 subjects in the Group 1 did not complete 4-week placebo lead-in period

FORWARD-3: Efficacy Analysis

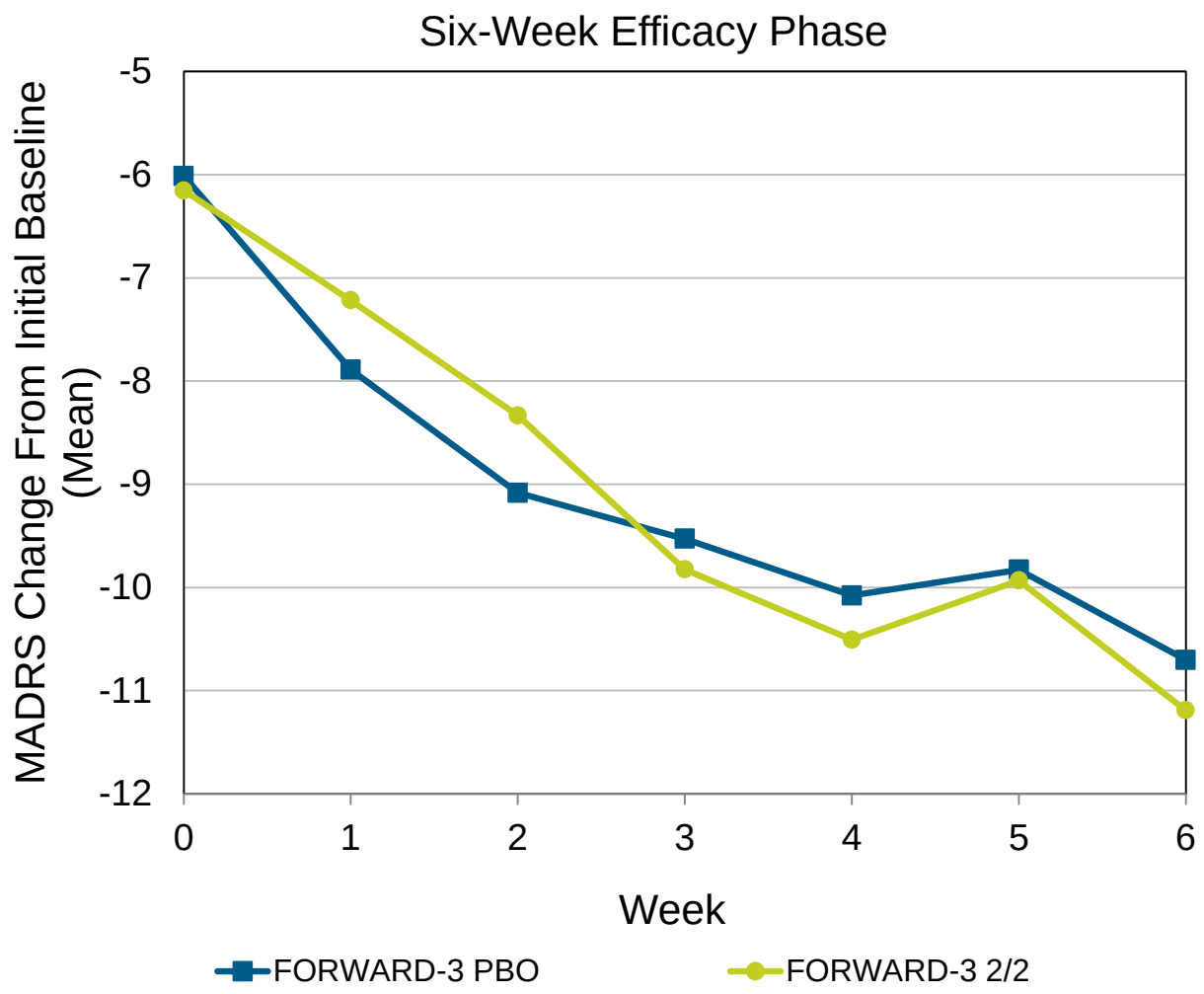


4-Week Lead-In

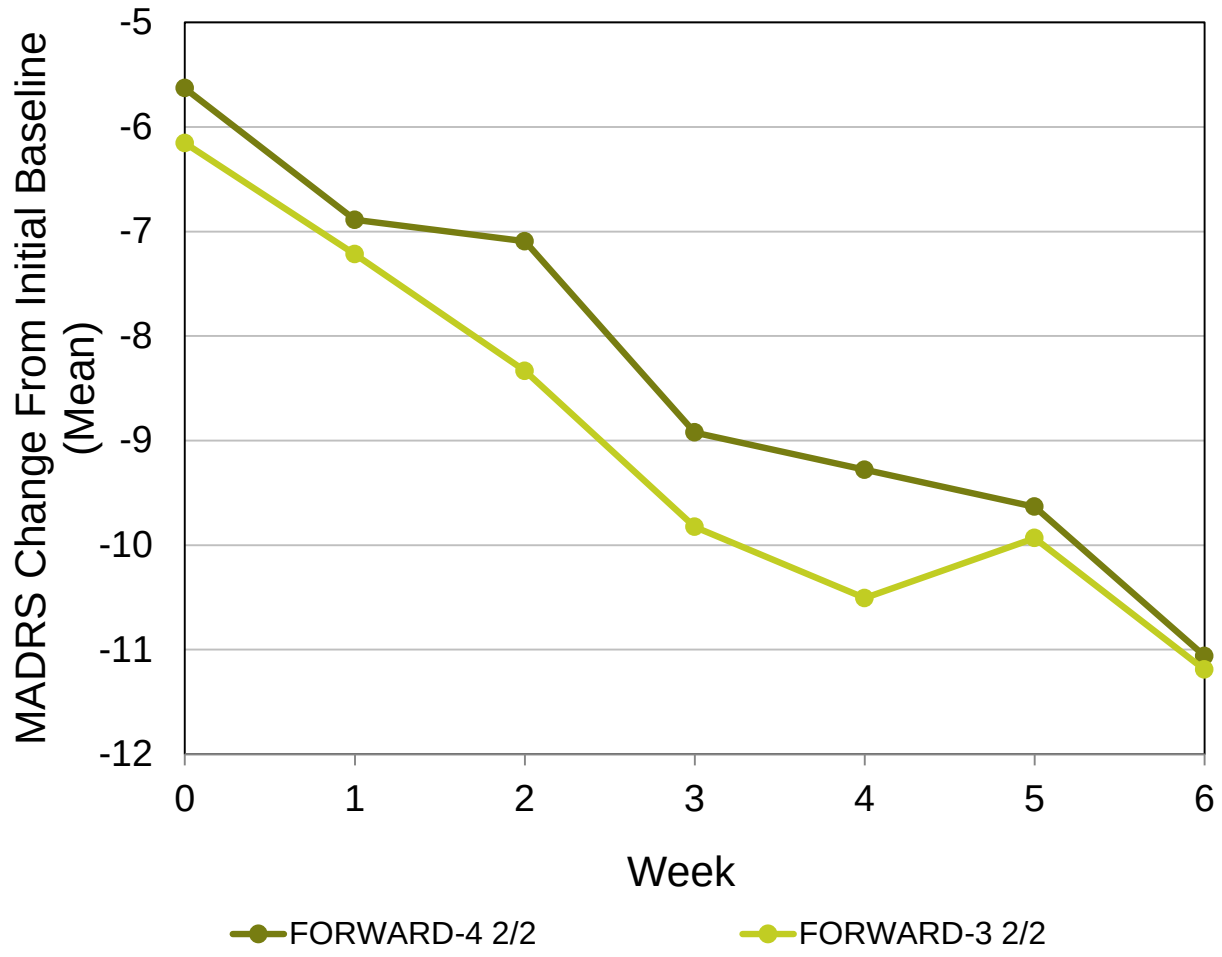
6-Week Efficacy Phase

25 subjects in Group 1 did not complete 4-week placebo lead-in period

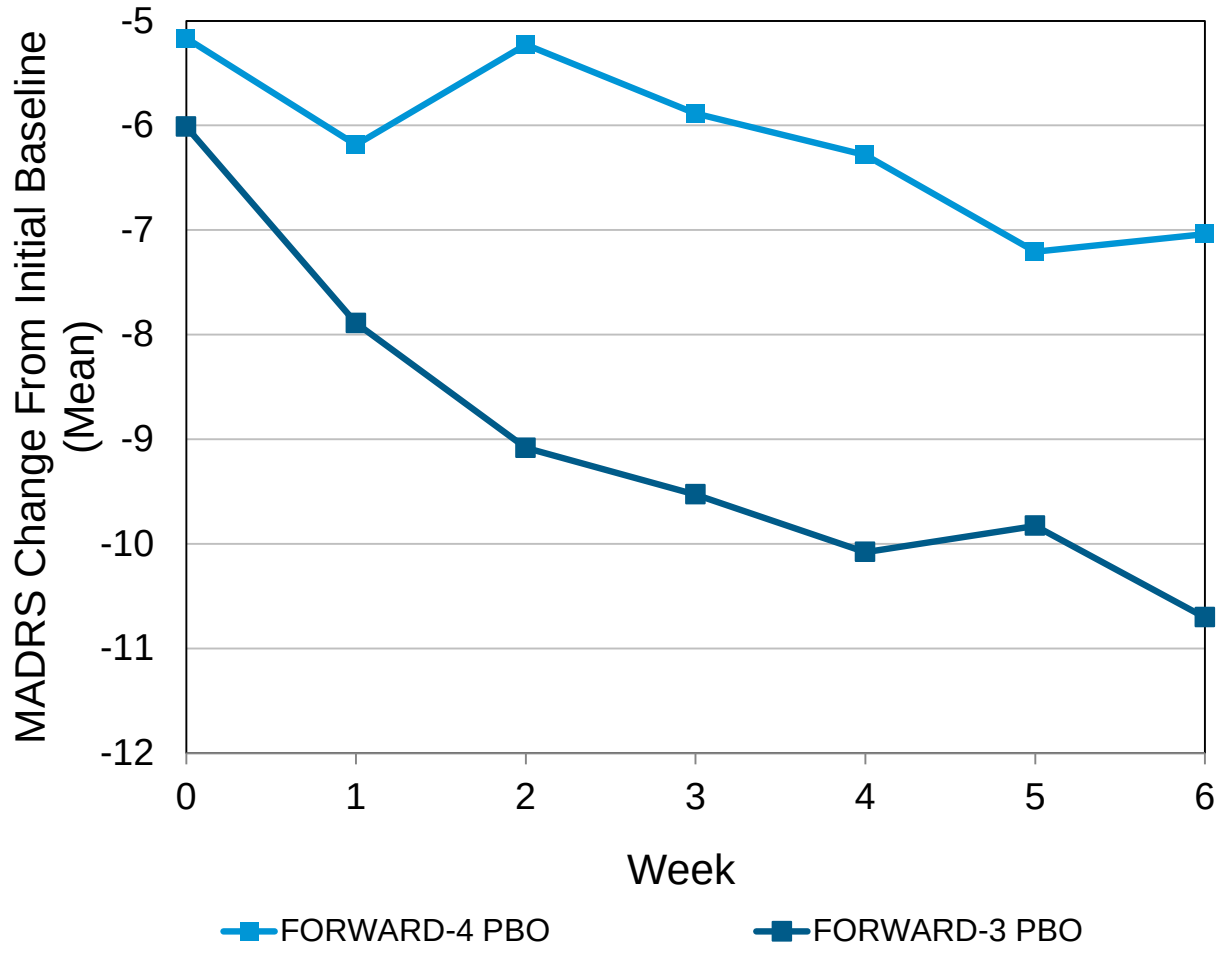
FORWARD-3: Efficacy Phase
Change in MADRS from Baseline



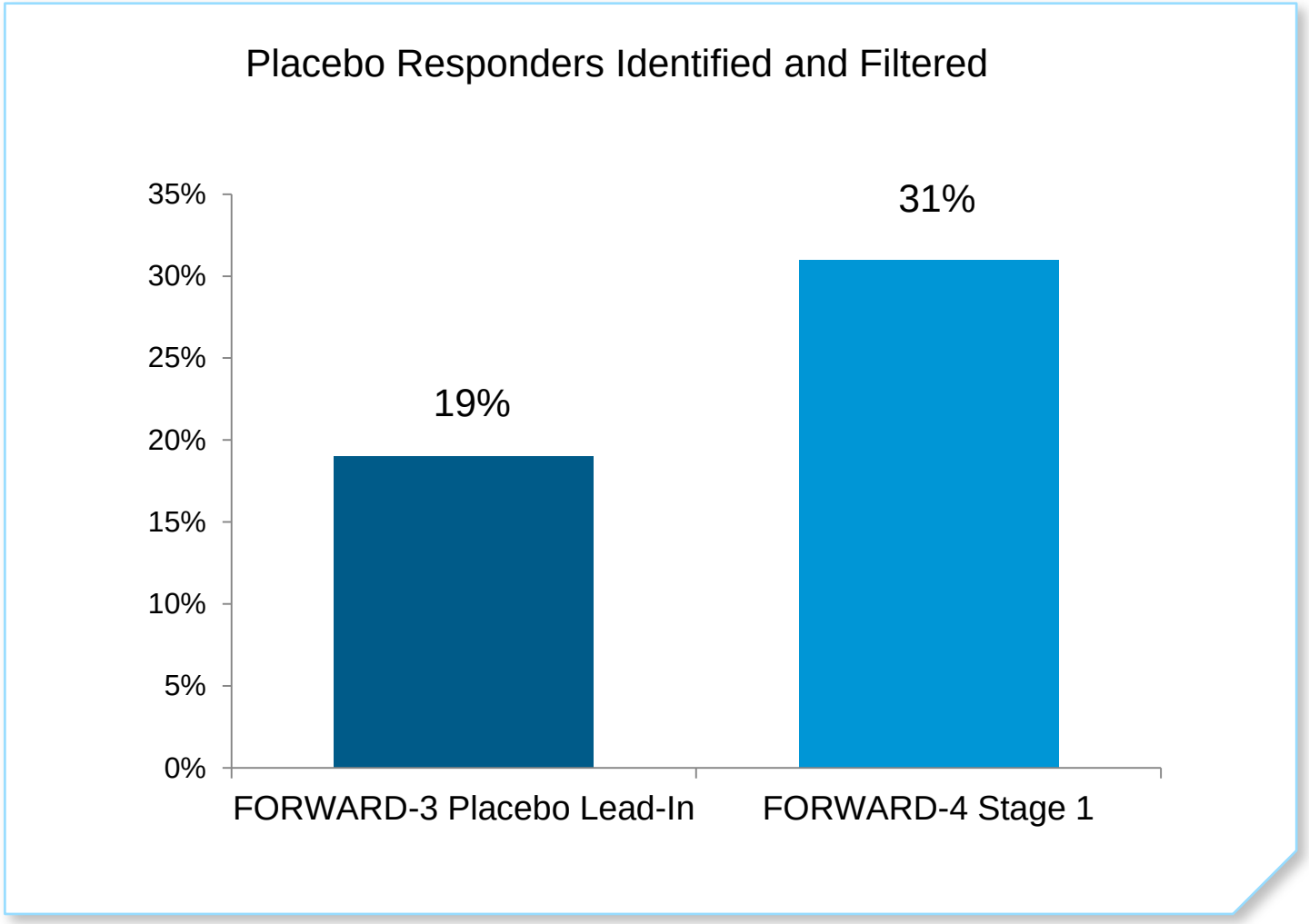
ALKS 5461 2/2 Dose: FORWARD-3 Efficacy Phase vs. FORWARD-4 Stage 2



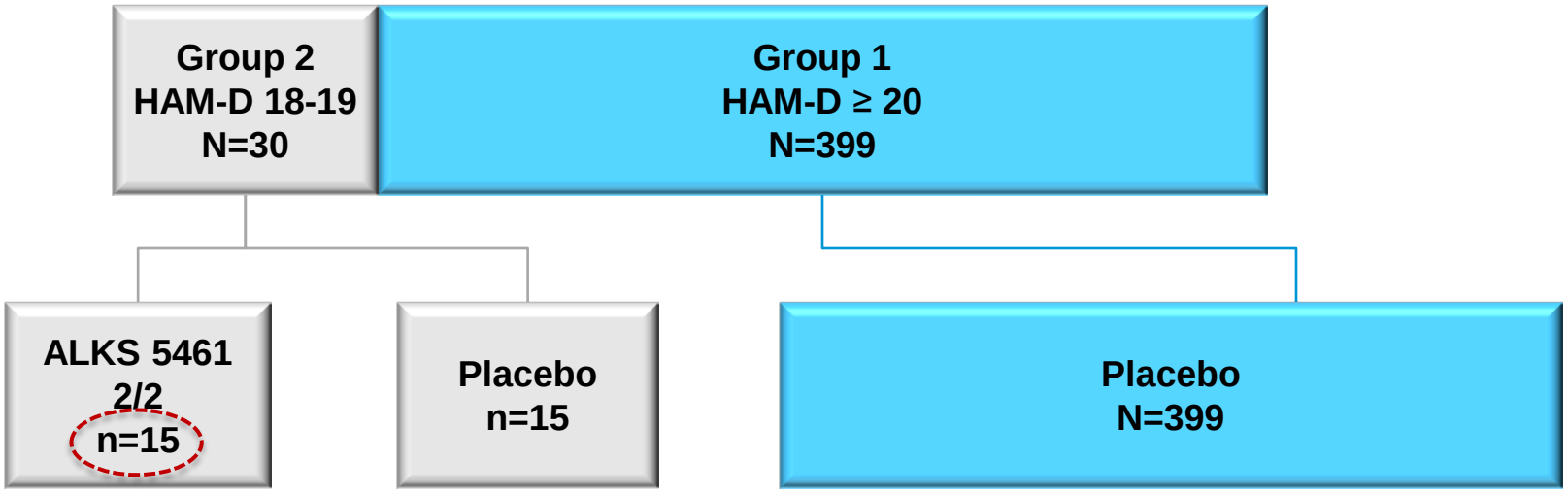
Placebo Treatment: FORWARD-3 Efficacy Phase vs. FORWARD-4 Stage 2



FORWARD-3 Was Less Effective Than FORWARD-4 in Removing Placebo Responders



FORWARD-3: Subject Flow



FORWARD-3 and FORWARD 4: Safety and Tolerability

- High study retention rates
- Adverse events were generally mild, transient and occurred around time of treatment initiation
  - FORWARD-3: Nausea, headache and fatigue
  - FORWARD-4: Nausea, headache and dizziness
- Safety and tolerability profile consistent with that reported in phase 2 and FORWARD-1 studies
- Data reinforced non-addictive profile with no evidence of withdrawal or pattern of adverse events indicative of abuse potential

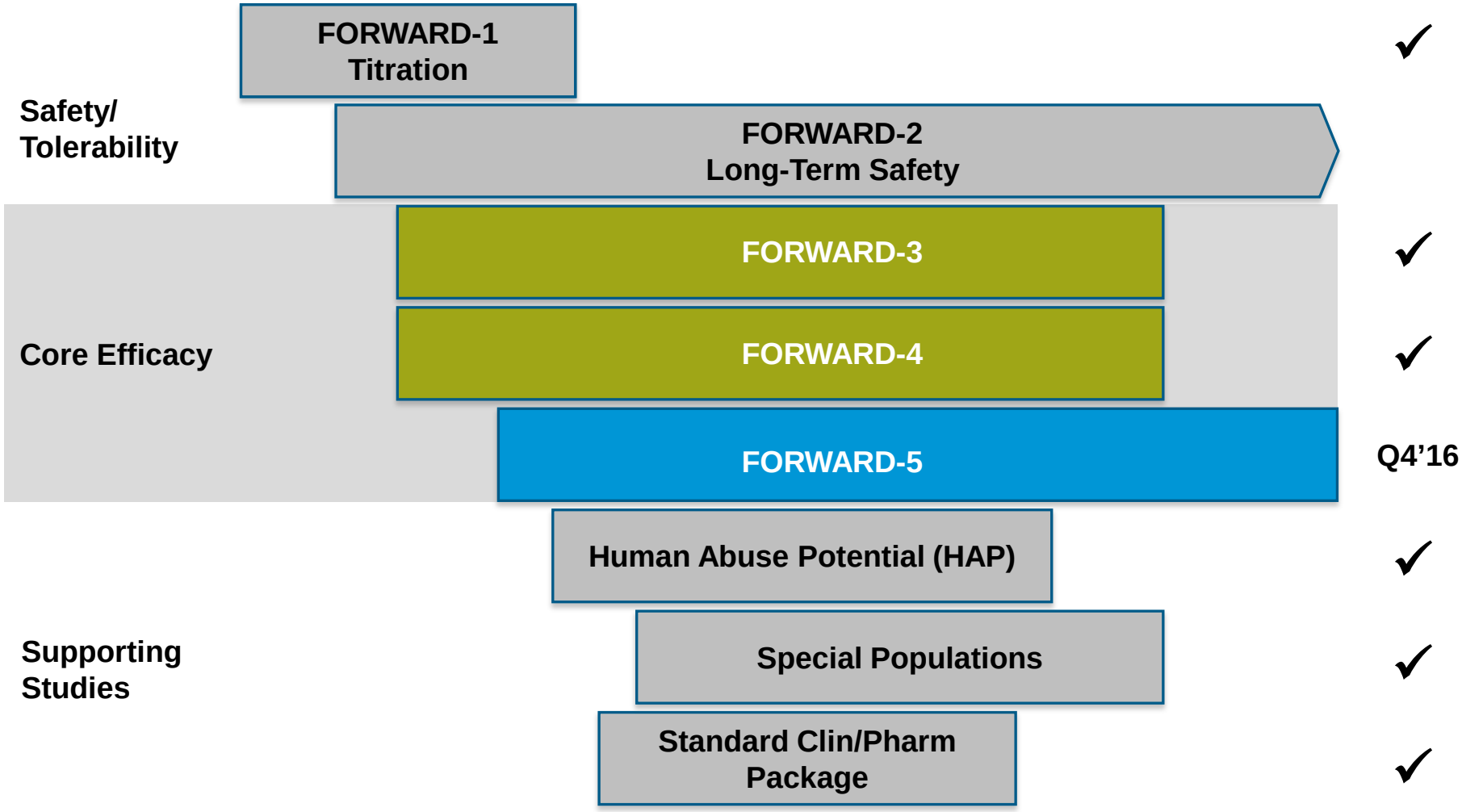
Key Learnings

- FORWARD-4 showed efficacy of ALKS 5461 2/2
  - Reinforces positive results from a previously reported phase 2 study
- FORWARD-4 design was superior to FORWARD-3 in identifying and filtering placebo responders
- ALKS 5461 2/2 had consistent safety, tolerability and efficacy profile in FORWARD-3 and FORWARD-4
- Learnings from FORWARD-3 and FORWARD-4 studies will be applied to ongoing FORWARD-5

FORWARD-5 Study Ongoing

- Applying key learnings from FORWARD-3 and FORWARD-4 to remaining portion of FORWARD-5
- SPCD consistent with FORWARD-4 design
- Evaluating 2mg/2mg and additional 1mg/1mg doses
- Expected enrollment: 400 subjects
- Topline data expected in Q4 2016

ALKS 5461: FORWARD Pivotal Program



Conclusions

Richard Pops, Chief Executive Officer

Q&A

www.alkermes.com