Vibrance-2: Study Design and Methods for a Phase 2, Randomised, Placebo-Controlled, Parallel Group Study Evaluating the Safety and Efficacy of ALKS 2680 in Patients With Narcolepsy Type 2

David Plante,[1] Ron Grunstein,[2] Giuseppe Plazzi,[3] Chad Ruoff,[4] Jandira Ramos,[5] Shifang Liu,[5] Sergey Yagoda,[5] Bhaskar Rege[5]

[1]University of Wisconsin School of Medicine and Public Health, UW Department of Psychiatry, Madison, WI, USA; [2]Woolcock Institute of Medical Research, Macquarie Park, Sydney, Australia; [3]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy; [4]Mayo Clinic Hospital, Division of Pulmonary Medicine, Phoenix, AZ, USA; [5]Alkermes, Inc., Waltham, MA, USA

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INTRODUCTION

- ALKS 2680 is a highly potent, orally bioavailable, and selective orexin 2 receptor (OX2R) agonist being developed as a once-daily treatment for narcolepsy[1]
- Targeting the orexin (also known as hypocretin) system may address daytime sleepiness across hypersomnolence disorders with orexin deficiency (narcolepsy type 1 [NT1]) and without orexin deficiency (eg, narcolepsy type 2 [NT2] and idiopathic hypersomnia [IH])[2]
- In a phase 1b study, single doses of ALKS 2680 were generally well tolerated among patients with NT1[3] (1, 3, and 8 mg), NT2 (5, 12, and 25 mg), or IH (5, 12, and 25 mg), and led to statistically significant, clinically meaningful improvements in sleep latency and improved patient-reported alertness
  - Phase 1b results in patients with NT2 are presented in Poster P200
  - Phase 1b results in patients with IH are presented in Poster P5070
  - These results demonstrate that a potent OX2R agonist can be effective in patients with or without orexin deficiency
- Results from the phase 1b study of patients with NT2 informed the range of doses to be assessed in the phase 2 Vibrance-2 study

OBJECTIVES

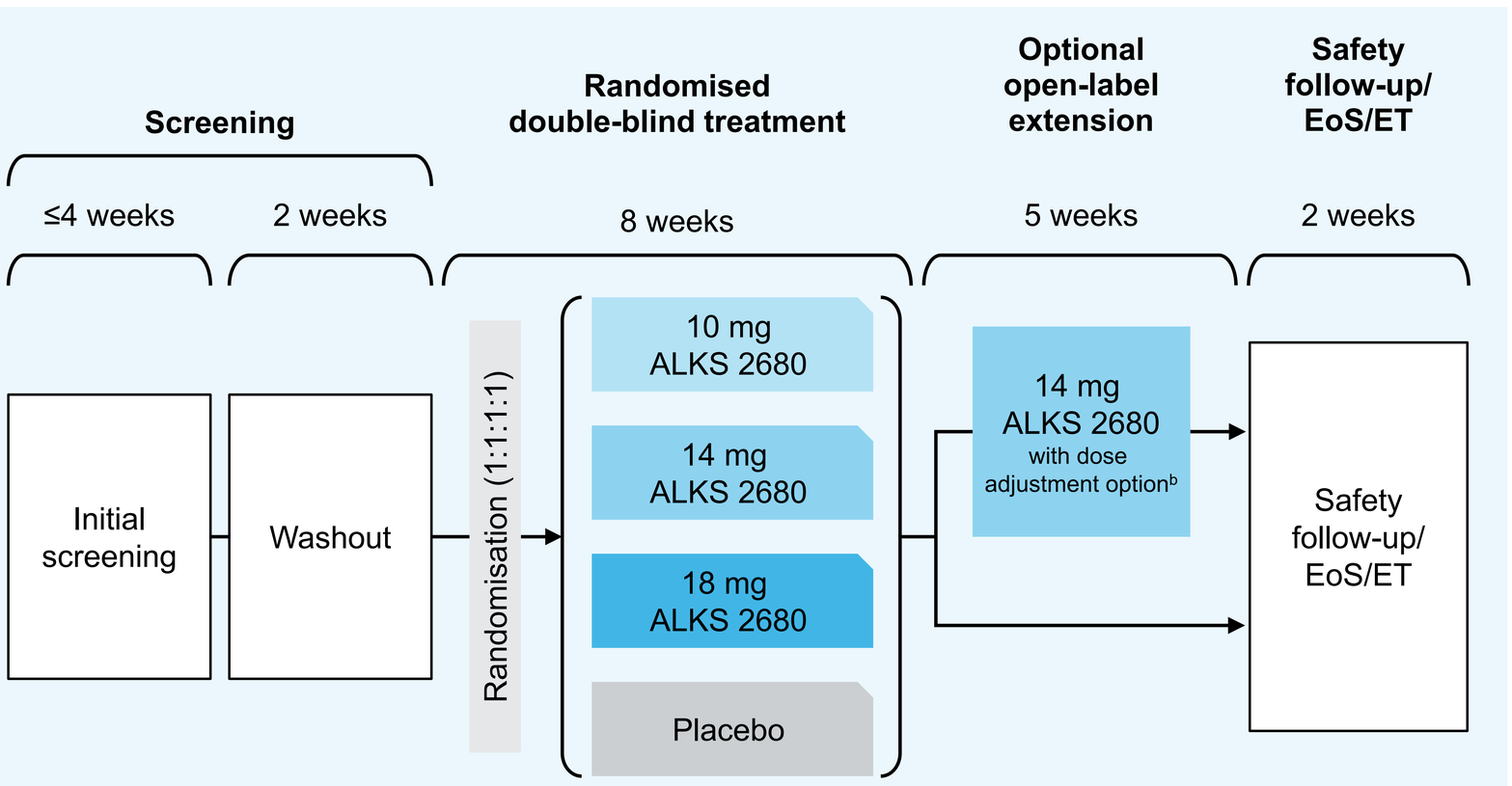
- The Vibrance-2 study (ClinicalTrials.gov identifier: NCT06555783) aims to assess the safety and efficacy of once-daily ALKS 2680 compared with placebo through 8 weeks of treatment in patients with NT2

METHODS

STUDY DESIGN

- Vibrance-2 is an ongoing, phase 2, placebo-controlled, parallel-group, dose-ranging study with a randomised double-blind treatment period and an open-label extension period (**Figure 1**)
- Following a 2-week washout period from prior narcolepsy medications, patients will be randomized 1:1:1:1 to receive placebo or ALKS 2680 once daily at doses of 10, 14, or 18 mg for 8 weeks
- The double-blind treatment period will be followed by an optional open-label extension period of 5 weeks

FIGURE 1: Vibrance-2 Study Design[a]



[a]The study is being conducted in the United States, Australia, and Europe. [b]Dose adjustments possible (up or down) during the first 2 weeks of the optional open-label extension period.
EoS = end of study; ET = early termination.

STUDY POPULATION

- Planned enrolment is approximately 80 patients with NT2
- Key inclusion and exclusion criteria are described in **Figure 2**

FIGURE 2: Key Inclusion and Exclusion Criteria[4a]

Inclusion Criteria	• Age 18 to ≤70 years
	• BMI ≥18 and ≤35 kg/m^2
	• Meets the diagnostic criteria of NT2 according to ICSD-3-TR guidelines[5] and:
	  ○ Has residual excessive daytime sleepiness[b]
	  ○ Has a mean sleep latency of ≤15 minutes across the 4 Maintenance of Wakefulness Test trials during screening
	• Willing and able to discontinue any medications prescribed for the management of narcolepsy symptoms for at least 14 days

Exclusion Criteria	**Presence of other significant comorbid medical conditions, including other sleep, cardiovascular, and psychiatric disorders**

[a]Additional criteria apply. Eligibility will be determined on an individual basis by the study investigator. [b]Epworth Sleepiness Scale score >12 at Visit 4.
BMI = body mass index; ICSD-3-TR = International Classification of Sleep Disorders – Third Edition, Text Revision; NT2 = narcolepsy type 2.

STUDY ENDPOINTS

- Primary, secondary, and exploratory endpoints are summarised in **Figure 3**

FIGURE 3: Study Endpoints[4]

Primary Endpoint
Change in mean sleep latency on the Maintenance of Wakefulness Test (MWT) from baseline to Week 8 by dose level

Secondary Endpoints
Change in Epworth Sleepiness Scale (ESS) from baseline to Week 8 by dose level

Treatment-emergent adverse events and other safety parameters by study period

Exploratory Endpoints
Sleep stages as measured by EEG power spectra

Patient- or clinician-reported outcomes, including:
- Karolinska Sleepiness Scale
- Narcolepsy Severity Scale
- Patient Global Impression of Severity
- Clinical Global Impression of Severity

EEG = electroencephalogram.

SUMMARY

- ALKS 2680 is currently the only OX2R agonist in phase 2 clinical development for both narcolepsy subtypes
- Vibrance-2 is evaluating once-daily ALKS 2680 over 8 weeks in patients with NT2, followed by optional open-label treatment
- To learn about participation or patient referrals, please visit vibrancestudies.com or clinicaltrials.gov/study/NCT06555783

Visit vibrancestudies.com

Visit Vibrance-2 at ClinicalTrials.gov

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