

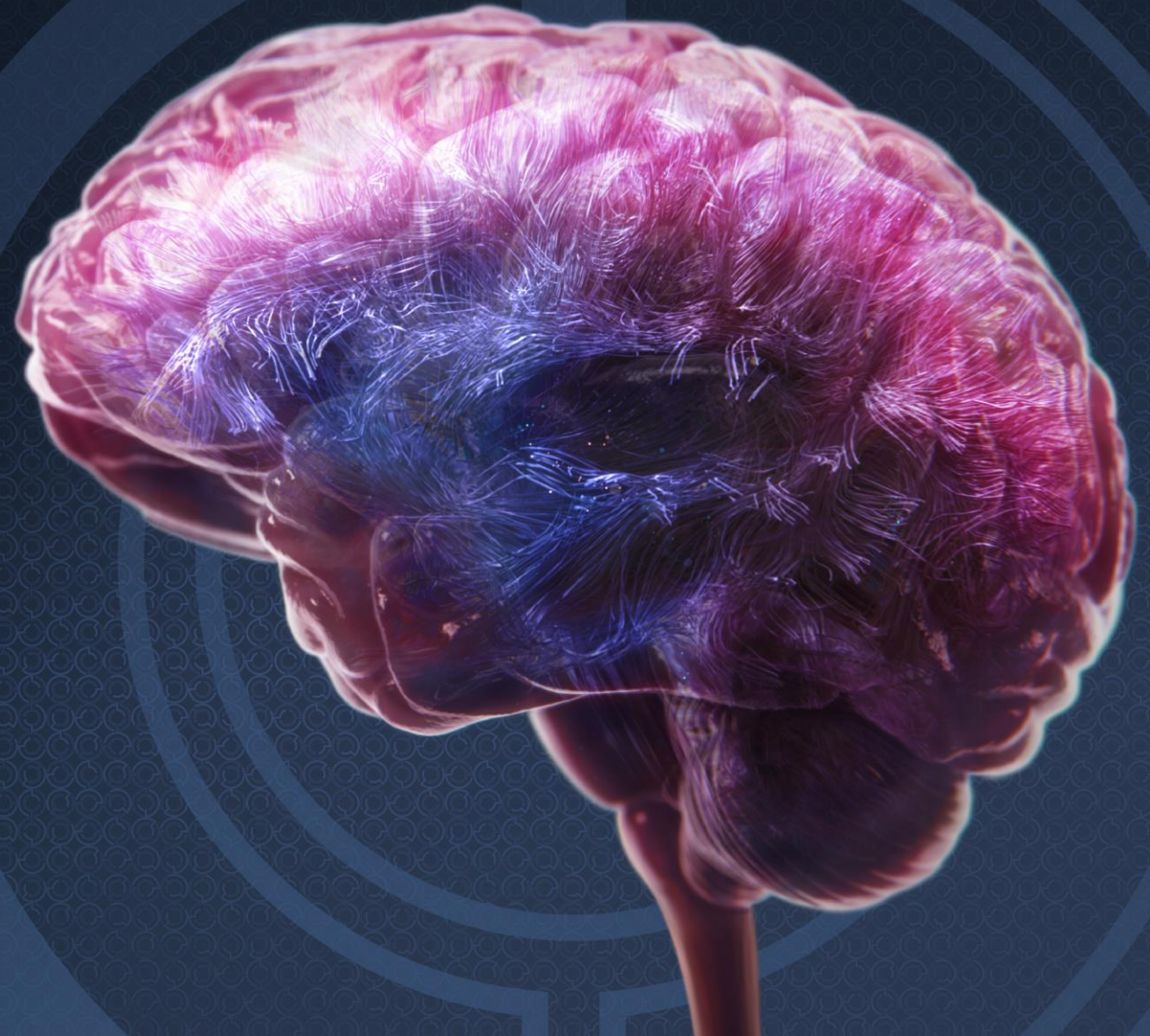
# DARIGABAT

## Phase 1 Topline Data in Acute Anxiety

*February 15, 2022*



Unraveling the mysteries of the brain





# Forward-Looking Statements

This presentation contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain.

Forward-looking statements in this presentation include, but are not limited to: statements about the potential attributes and benefits of our product candidates, including the ability of darigabat to achieve anxiolytic activity while minimizing side effects, to be a daily maintenance treatment and to transform the treatment paradigm in anxiety; the format and timing of our product development activities and clinical trials, including the timing of the Phase 2 proof-of-concept trial of darigabat in focal epilepsy and advancing development of darigabat in anxiety-related disorders; the ability to compete with other companies currently marketing or engaged in the development of treatments for relevant indications; the size and growth potential of the markets for product candidates and ability to serve those markets; and the rate and degree of market acceptance of product candidates, if approved.

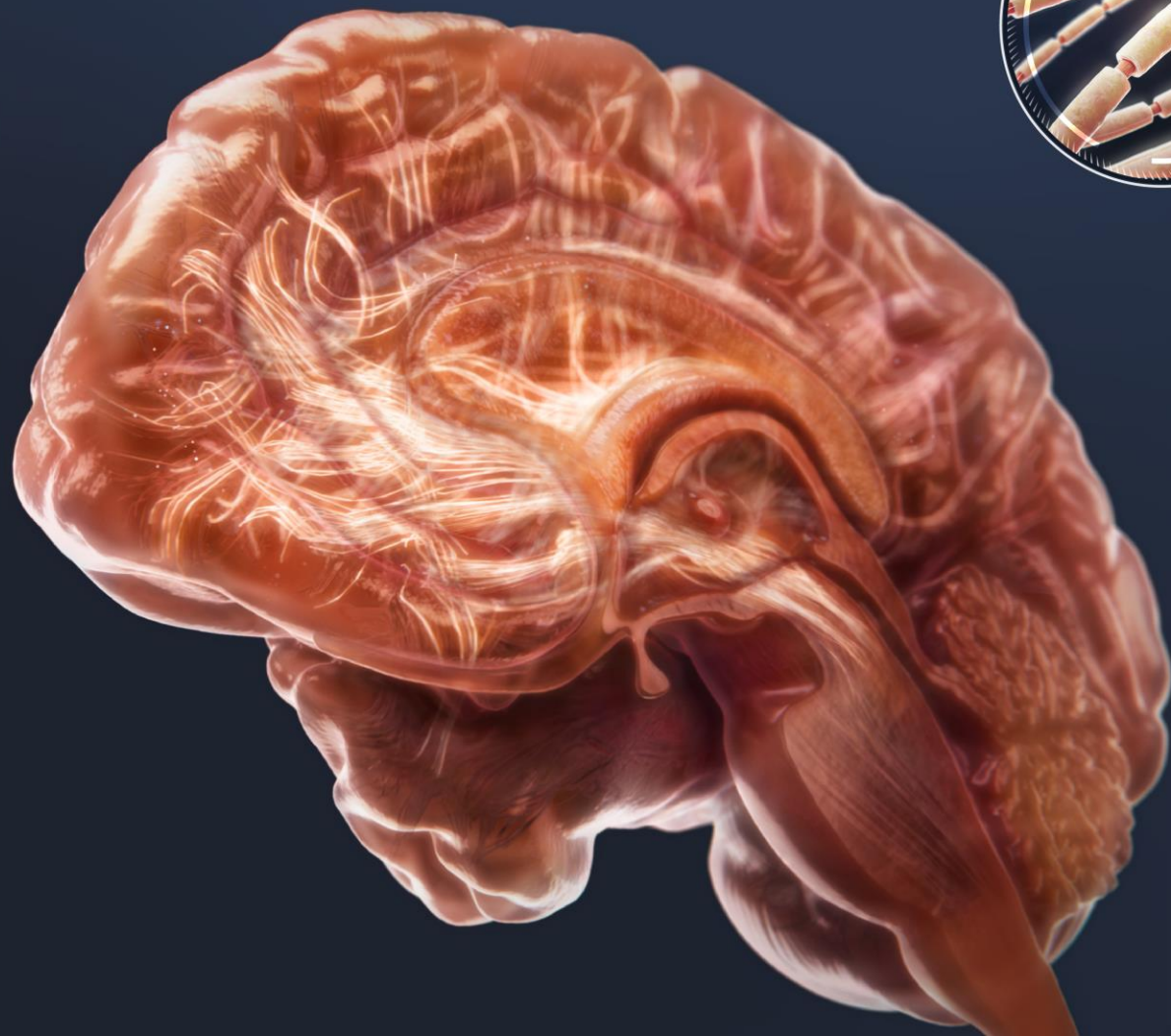
We cannot assure you that the forward-looking statements in this presentation will prove to be accurate. Furthermore, if the forward-looking statements prove to be inaccurate, the inaccuracy may be material. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties, including, among others: that clinical trial results may not be favorable; uncertainties inherent in the product development process (including with respect to the timing of results and whether such results will be predictive of future results); the impact of COVID-19 on the timing, progress and results of ongoing or planned clinical trials; other impacts of COVID-19, including operational disruptions or delays or to our ability to raise additional capital; whether and when, if at all, our product candidates will receive approval from the FDA or other regulatory authorities, and for which, if any, indications; competition from other biotechnology companies; uncertainties regarding intellectual property protection; and other risks identified in our SEC filings, including those under the heading "Risk Factors" in our Quarterly Report on Form 10-Q filed with the SEC on November 10, 2021 and our subsequent SEC filings.

In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The forward-looking statements in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation.



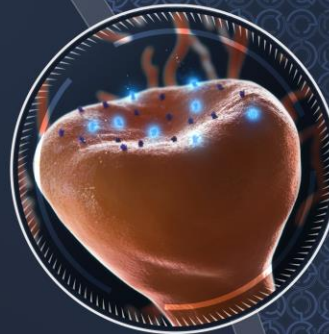
# CEREVEL: Unraveling the Mysteries of the Brain

A Differentiated Approach to Treating Neuroscience Diseases



## Targeted Neurocircuitry

Cerevel unlocks new treatment opportunities by precisely identifying and targeting the neurocircuit that underlies a given neuroscience disease.



## Receptor Sub-Type Selectivity

Cerevel is selectively targeting only the receptor subtype(s) related to the disease physiology, to minimize undesirable off-target effects while maximizing activity.



## Differentiated Pharmacology

Cerevel designs full and partial agonists, antagonists, and allosteric modulators that can precisely fine-tune the receptor pharmacology and neurocircuit activity without over-activation or over-suppression of the endogenous physiologic range.



# Darigabat has Potential for Anxiolytic Activity, Improved Side Effect Profile and Chronic Dosing

## Darigabat

Potential to become first-line and adjunct therapy

**Targeted GABA<sub>A</sub>  $\alpha$  2/3/5 Receptor Selectivity**

Benzodiazepine-like Activity

Improved Tolerability

Potential for Reduced Abuse Liability

High Unmet Need

**>370M<sup>1</sup>**  
Patients Worldwide with Anxiety Disorders

**<50%**  
Remission Rate<sup>2</sup>

No new medications in over 10 years

Benzos are highly efficacious, but...

Indicated for episodic use

Poor Tolerability

Potential for Abuse

Withdrawal

**Potential as daily maintenance therapy with improved side effect profile and tolerability may expand use vs. traditional benzodiazepines**

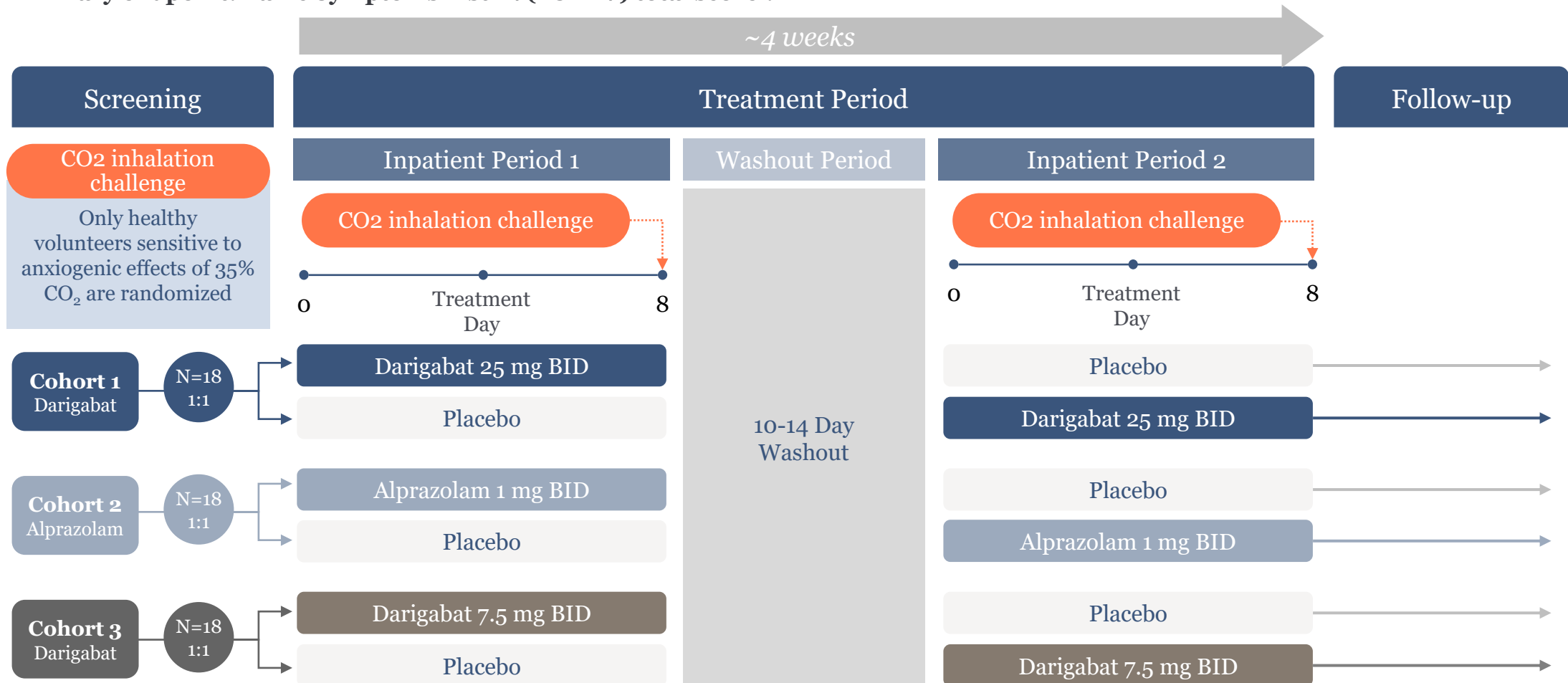


# **Phase 1 Healthy Volunteer Trial in Acute Anxiety**



# Phase 1 Trial Design Evaluating Darigabat in Acute Anxiety

Randomized, double-blind, placebo- and active-controlled crossover design with multiple doses over 8 days.  
Primary endpoint: Panic Symptoms List-IV(PSL-IV) total score<sup>1</sup>.



<sup>1</sup> The Panic Symptom List (PSL-IV) total score includes 13 symptoms scored across a range of 0 (absent) to 4 (very intense) that is used to assess panic anxiety. Liebold et al. Trans Psychiatry. 2016.; Bailey et al. J Psychopharm. 2011.; Malizia et al. Arch Gen Psychiatry. 1998.; Salvatore et al. Translational Psychiatry 2020.

# Subject Disposition

| Number of Subjects    | Cohort 1<br>( Darigabat 25 mg<br>BID / PBO) | Cohort 2<br>(Alprazolam 1 mg<br>BID/PBO) | Cohort 3<br>( Darigabat 7.5 mg<br>BID / PBO) | Overall |
|-----------------------|---|--|--|---------|
| Screened              |   |  |  | 241     |
| Randomized            | 18  | 20                                       | 18   | 56      |
| Discontinued          | 0   | 2  | 0  | 2       |
| Adverse Event         | 0   | 1 <sup>a</sup>                           | 0  | 1       |
| Withdrawal by Subject | 0   | 1 <sup>b</sup>                           | 0  | 1       |
| Completed Period      |   |  |  |         |
| Period 1              | 18  | 20                                       | 18   | 56      |
| Period 2              | 18  | 18                                       | 18   | 54      |

<sup>a</sup> Subject discontinued during placebo treatment period (Period 2) due to adverse event of COVID-19 infection.

<sup>b</sup> Subject withdrew during placebo treatment period (Period 2).

# Demographic Characteristics\*

|   | Cohort 1 N= 18<br>(Darigabat 25 mg BID / PBO) | Cohort 2 N= 20<br>(Alprazolam 1 mg BID / PBO) | Cohort 3 N= 18<br>( Darigabat 7.5 mg BID / PBO) | Overall<br>N= 56 |
|---|---|---|---|------------------|
| Age (years) at Screening                          |   |   |   |                  |
| Mean ± SD   | 26.4 ± 9.7                                    | 22.9 ± 4.7                                    | 27.7 ± 8.0                                      | 25.5 ± 7.8       |
| Median  | 23.0  | 20.5  | 25.5  | 24.0             |
| Sex N (%)   |   |   |   |                  |
| Male  | 6 (33%)                                       | 6 (30%)                                       | 12 (67%)  | 24 (43%)         |
| Female  | 12 (67%)                                      | 14 (70%)                                      | 6 (33%)   | 32 (57%)         |
| Race N (%)  |   |   |   |                  |
| Asian   | 0   | 0   | 1 (6%)  | 1 (2%)           |
| Black   | 0   | 1 (5%)  | 0   | 1 (2%)           |
| White   | 17 (94%)                                      | 18 (90%)                                      | 15 (83%)  | 50 (89%)         |
| Other or Multiple                                 | 1 (6%)  | 1 (5%)  | 2 (11%)   | 4 (7%)           |
| Weight (kg) <sup>a</sup>                          |   |   |   |                  |
| Mean ± SD   | 69.6 ± 14.3                                   | 68.8 ± 12.2                                   | 73.1 ± 12.0                                     | 70.4 ± 12.8      |
| Body Mass Index (kg/m <sup>2</sup> ) <sup>a</sup> |   |   |   |                  |
| Mean ± SD   | 23.6 ± 3.1                                    | 22.9 ± 2.9                                    | 23.0 ± 3.1                                      | 23.1 ± 3.0       |
| Median  | 23.2  | 22.4  | 22.4  | 22.5             |

\*Study population characteristics consistent with that expected of healthy volunteers.

Racial distribution reflects local population of the single site in the Netherlands.

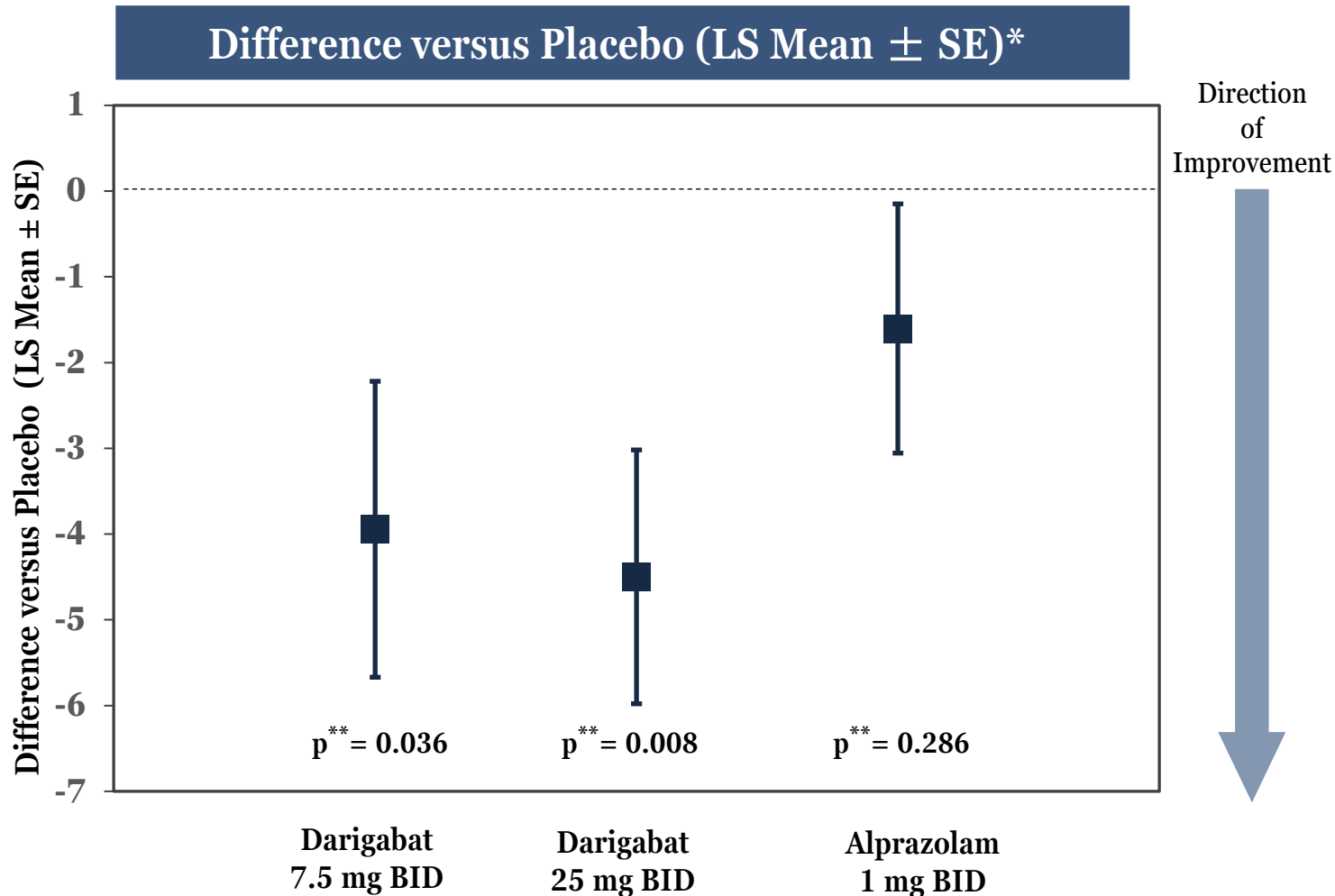
<sup>a</sup>At screening visit.



# Pharmacodynamic Results



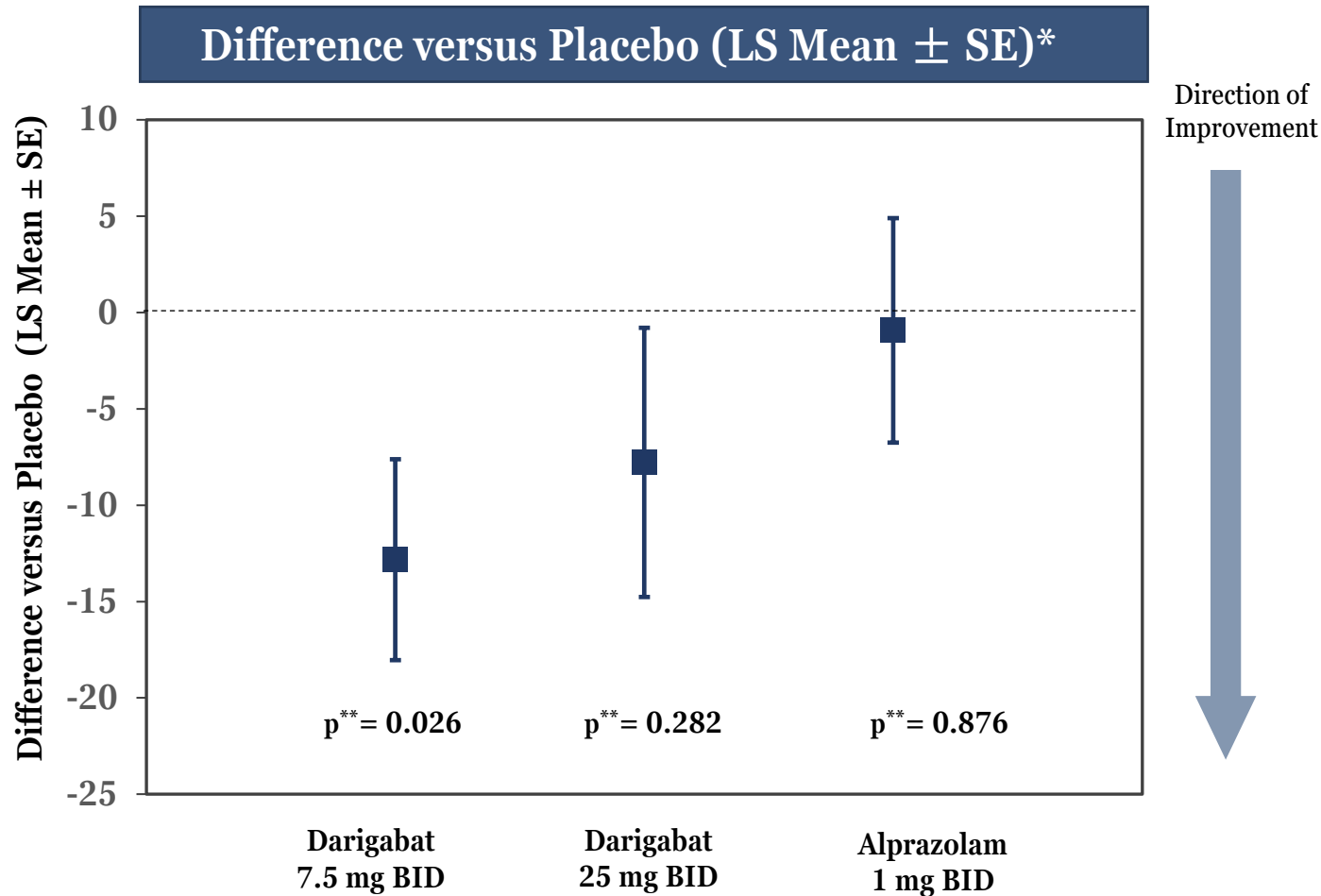
# Primary Endpoint: Change in Panic Symptoms List Score (PSL-IV) at Day 8



- **Darigabat 7.5 mg BID:**  
3.9-point improvement versus placebo at the end of 8-day treatment (9.9 on 7.5 mg BID versus 13.8 on placebo in PSL-IV total score increase following CO<sub>2</sub> challenge) with p<sup>\*\*</sup>=0.036
- **Darigabat 25 mg BID:**  
4.5-point improvement versus placebo at the end of 8-day treatment (12.5 on 25 mg BID versus 17.0 on placebo in PSL-IV total score increase following CO<sub>2</sub> challenge) with p<sup>\*\*</sup>=0.008
- **Alprazolam 1 mg BID:**  
1.6-point improvement versus placebo at the end of 8-day treatment (14.5 on alprazolam 1 mg BID versus 16.1 on placebo in PSL-IV total score increase following CO<sub>2</sub> challenge) with p<sup>\*\*</sup>=0.286



## Secondary Endpoint: Change in Fear Visual Analog Scale (VAS) at Day 8



- **Darigabat 7.5 mg BID:**  
12.8-point improvement versus placebo at the end of 8-day treatment (23.6 on 7.5 mg BID versus 36.4 on placebo in VAS Fear score increase following CO<sub>2</sub> challenge) with p<sup>\*\*</sup>=0.026
- **Darigabat 25 mg BID:**  
7.8-point improvement versus placebo at the end of 8-day treatment (33.2 on 25 mg BID versus 41.0 on placebo in VAS Fear score increase following CO<sub>2</sub> challenge) with p<sup>\*\*</sup>=0.282
- **Alprazolam 1 mg BID:**  
0.9-point improvement versus placebo at the end of 8-day treatment (42.5 on alprazolam 1 mg BID versus 43.4 on placebo in VAS Fear score increase following CO<sub>2</sub> challenge) with p<sup>\*\*</sup>=0.876



# Safety & Tolerability



# Summary of Treatment Emergent Adverse Events (TEAE)

|   | Number (%) of Subjects*         |                                  |                      |                     |
|---|---------------------------------|----------------------------------|----------------------|---------------------|
|   | Placebo<br>(Combined)<br>(N=56) | Alprazolam<br>1 mg BID<br>(N=20) | Darigabat            |                     |
|   |                                 |                                  | 7.5 mg BID<br>(N=18) | 25 mg BID<br>(N=18) |
| Subjects with TEAE                            | 28 (50%)                        | 18 (90%)                         | 13 (72%)             | 17 (94%)            |
| Mild  | 26 (46%)                        | 18 (90%)                         | 12 (67%)             | 16 (89%)            |
| Moderate                                      | 1 (2%)                          | 0                                | 1 (6%)               | 1 (6%)              |
| Severe  | 1 (2%)                          | 0                                | 0                    | 0                   |
| Subjects with Serious TEAE                    | 0                               | 0                                | 0                    | 0                   |
| Subjects with TEAE Leading to Discontinuation | 1 (2%)                          | 0                                | 0                    | 0                   |
| Subjects with TEAE Related to IMP             | 15 ( 27%)                       | 17 ( 85%)                        | 13 ( 72%)            | 17 ( 94%)           |

\* Number of subjects with at least 1 AE reported

# Adverse Events with Incidence $\geq 10\%^*$ and $>$ Placebo with Any Active Treatments (1 of 2)

| Preferred Term           | Number (%) of Subjects          |                                  |                      |                     |
|--------------------------|---------------------------------|----------------------------------|----------------------|---------------------|
|                          | Placebo<br>(Combined)<br>(N=56) | Alprazolam<br>1 mg BID<br>(N=20) | Darigabat            |                     |
|                          |                                 |                                  | 7.5 mg BID<br>(N=18) | 25 mg BID<br>(N=18) |
| Bradyphrenia             | 1 (2%)                          | 1 (5%)                           | 2 (11%)              | 9 (50%)             |
| Dizziness                | 1 (2%)                          | 3 (15%)                          | 6 (33%)              | 8 (44%)             |
| Somnolence               | 2 (4%)                          | 10 (50%)                         | 4 (22%)              | 8 (44%)             |
| Disturbance in attention | 0                               | 0                                | 2 (11%)              | 6 (33%)             |
| Fatigue                  | 6 (11%)                         | 11 (55%)                         | 5 (28%)              | 5 (28%)             |
| Headache                 | 12 (21%)                        | 0                                | 3 (17%)              | 5 (28%)             |
| Balance disorder         | 1 (2%)                          | 2 (10%)                          | 2 (11%)              | 3 (17%)             |
| Abdominal pain upper     | 0                               | 0                                | 0                    | 2 (11%)             |
| Dizziness postural       | 0                               | 1 (5%)                           | 0                    | 2 (11%)             |
| Euphoric mood            | 0                               | 0                                | 2 (11%)              | 2 (11%)             |
| Insomnia                 | 0                               | 1 (5%)                           | 0                    | 2 (11%)             |

\* Equivalent to  $\geq 2$  subjects out of 18 or 20



## Adverse Events with Incidence $\geq 10\%^*$ and $>$ Placebo with Any Active Treatments (2 of 2)

| Preferred Term           | Number (%) of Subjects          |                                  |                      |                     |
|--------------------------|---------------------------------|----------------------------------|----------------------|---------------------|
|                          | Placebo<br>(Combined)<br>(N=56) | Alprazolam<br>1 mg BID<br>(N=20) | Darigabat            |                     |
|                          |                                 |                                  | 7.5 mg BID<br>(N=18) | 25 mg BID<br>(N=18) |
| Musculoskeletal pain     | 0                               | 0                                | 0                    | 2 (11%)             |
| Nausea                   | 3 (5%)                          | 2 (10%)                          | 3 (17%)              | 1 (6%)              |
| Feeling of relaxation    | 0                               | 0                                | 3 (17%)              | 0                   |
| Drug withdrawal syndrome | 0                               | 3 (15%)                          | 0                    | 0                   |
| Nasopharyngitis          | 1 (2%)                          | 0                                | 2 (11%)              | 0                   |
| Dry mouth                | 1 (2%)                          | 0                                | 2 (11%)              | 0                   |
| Abnormal dreams          | 0                               | 2 (10%)                          | 0                    | 0                   |
| Listless                 | 0                               | 2 (10%)                          | 0                    | 0                   |
| Dysmenorrhoea            | 2 (4%)                          | 2 (10%)                          | 0                    | 0                   |

\* Equivalent to  $\geq 2$  subjects out of 18 or 20

# Conclusions

- **Pharmacodynamic Results**

- ❑ Both doses of darigabat exhibited clinically meaningful and statistically significant anxiolytic activity compared to placebo based on the primary endpoint, PSL-IV total score
- ❑ Results were supported by improvements in the secondary endpoint, VAS Fear score
- ❑ Positive control alprazolam 1 mg BID exhibited anxiolytic activity compared to placebo in line with expectations for this model

- **Safety & Tolerability**

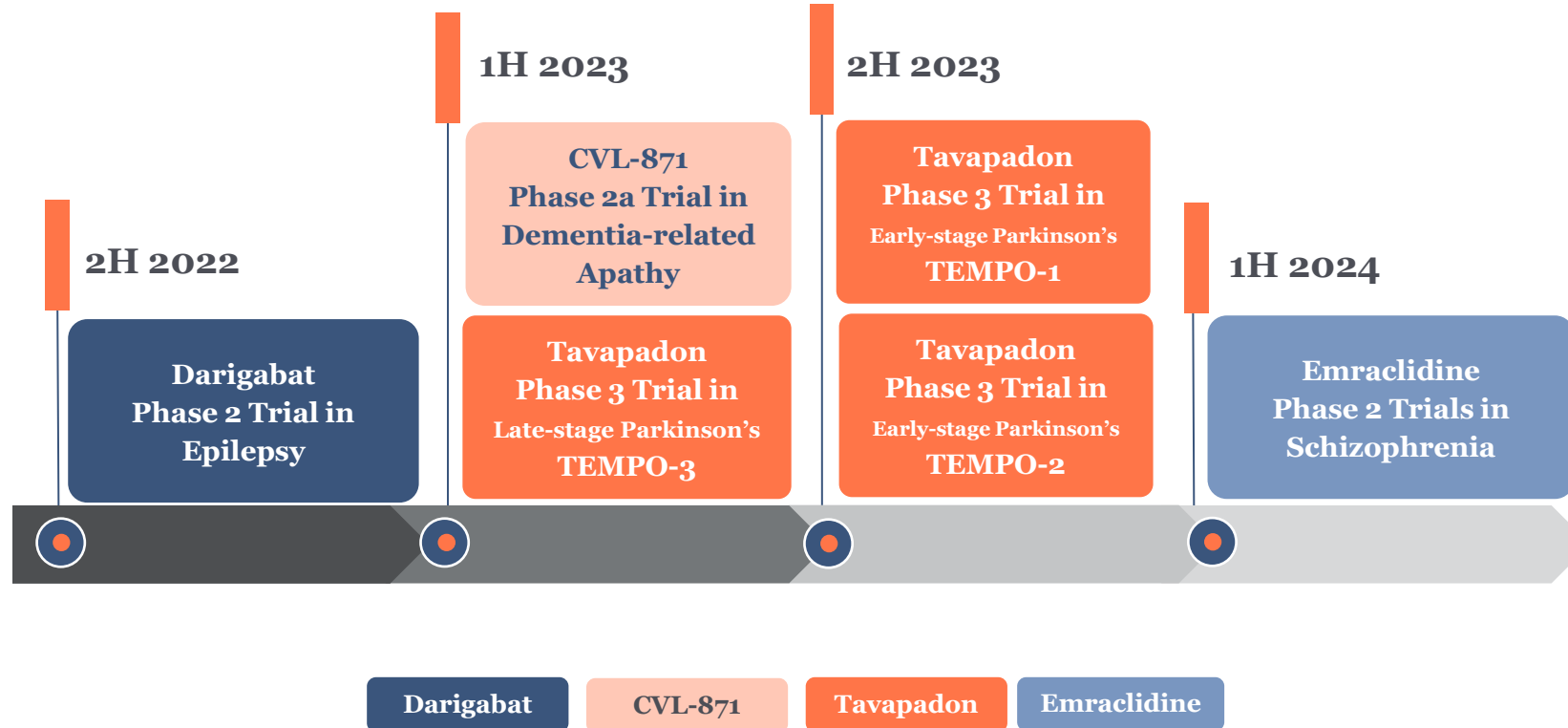
- ❑ Darigabat was generally well-tolerated in this trial, with no serious adverse events and no discontinuations in the darigabat cohorts

- **Conclusions and Next Steps**

- ❑ Trial demonstrated the anxiolytic potential of darigabat based on reduction of acute anxiety/panic evoked by CO<sub>2</sub> inhalation in healthy subjects
- ❑ Cerevel intends to pursue development of darigabat in anxiety-related disorders



# Key Milestones – Upcoming Data Readouts





Thank You