Poster 7

BHV-7000, a Novel, Selective Kv7 Potassium Channel Activator, in Late-Stage Development for Major Depressive Disorder and Bipolar Disorder

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INTRODUCTION

- Current treatment options for major depressive disorder and bipolar disorder are limited by low efficacy and adverse events
- Among patients with major depressive disorder, 70% have inadequate response to first-line selective serotonin reuptake inhibitors, and 33% remain refractory to second- and third-line options[1]
- 50% to 60% of patients with bipolar disorder and major depressive disorder, respectively, are medication nonadherent, with discontinuations most commonly due to adverse effects[2-4]
- In the last 20 years, no new mood stabilizer has been approved for bipolar disorder, with the only new agents being antipsychotics[5]
- Kv7.2/7.3 potassium channels play a key role in modulating neural hyperexcitability that underpins mood disorders[6-8]
- Kv7 activation normalizes the pathological hyperexcitability that contributes to depression and has demonstrated efficacy in multiple preclinical models[6-8]
- Clinical proof-of-concept studies with Kv7 activators have demonstrated antidepressant activity and provide support for Kv7 activation as a novel treatment for depression and anhedonia[9-11]
- The Kv7 channel is also a compelling target for bipolar disorder; human genetics link Kv7 to risk of bipolar disorder, and preclinical models show Kv7 activation corrects disease-related phenotypes and behaviors[12]
- BHV-7000 is a novel, small molecule, selective activator of the Kv7.2/7.3 potassium channel and has improved motivation and impulsivity in preclinical studies[13,14]
- In phase 1 studies, BHV-7000 was safe and well tolerated, with low rates of central nervous system adverse events (ie, no cases of somnolence)[15]

OBJECTIVE

- To describe ongoing late-stage registrational phase 2/3 studies evaluating the clinical efficacy and safety of BHV-7000 in major depressive disorder (NCT06419608) and bipolar disorder (NCT06419582)

CONCLUSIONS

- A significant need exists for new medications with novel mechanisms of action and differentiated tolerability and efficacy for major depressive disorder and bipolar disorder
- BHV-7000 is a selective Kv7 potassium channel activator in late-stage development for major depressive disorder and bipolar disorder
- BHV-7000 offers a novel and differentiated mechanism of action with the potential for efficacy and improved tolerability among existing treatments for major depressive disorder and bipolar disorder
- Both studies are ongoing at multiple sites across the United States

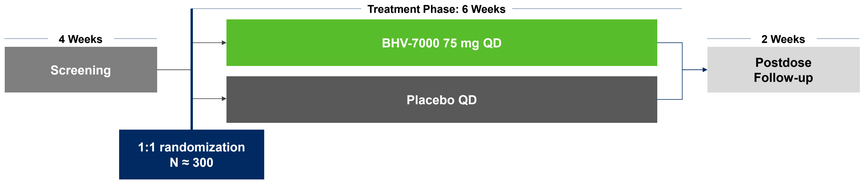
Please scan the QR code for more information on the ongoing clinical trials with BHV-7000

METHODS

Phase 2 Study in Major Depressive Disorder

- A phase 2 multicenter, randomized, double-blind, placebo-controlled study of BHV-7000 monotherapy for the treatment of major depressive disorder
- Approximately 300 participants will be randomized 1:1 to BHV-7000 75 mg or placebo once daily and treated for 6 weeks (**Figure 1**); endpoints are listed in **Table 1**

Figure 1. Phase 2 Study of BHV-7000 in Major Depressive Disorder



Select Inclusion Criteria	• Aged 18-75 years at time of consent • Experiencing a moderate to severe episode of depression with anhedonia for at least 2 months (HAM-D ≥ 20, SHAPS ≥ 20) • Willingness to discontinue all other medications for depression before entering the study
Select Exclusion Criteria	• History of bipolar disorder, schizophrenia, or other neuropsychiatric conditions that may interfere with the conduct of the study • Taking > 2 medications (other than benzodiazepines and medications for insomnia) to treat depression at screening

HAM-D, Hamilton Depression Rating Scale; QD, once daily; SHAPS, Snaith-Hamilton Pleasure Scale.

Table 1. Endpoints in Major Depressive Disorder

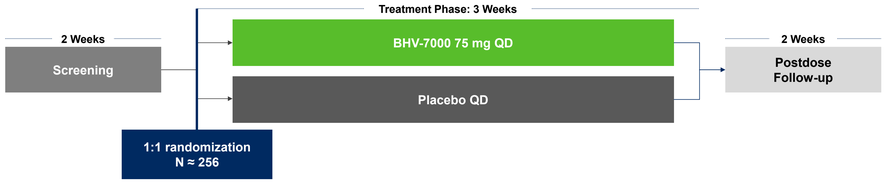
Primary endpoint	• Change in Montgomery-Åsberg Depression Rating Scale (MADRS) total score: baseline to week 6
Key secondary endpoints	• Change in CGI-S scale total score: baseline to week 6 • Change in SHAPS total score: baseline to week 6 • Change in MADRS total score: baseline to week 1 • Change in SHAPS total score: baseline to week 1 • Q-LES-Q-SF total score: baseline to week 6

CGI-S, Clinical Global Clinical Impression–Severity; MADRS, Montgomery-Åsberg Depression Rating Scale; Q-LES-Q-SF, Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form; SHAPS, Snaith-Hamilton Pleasure Scale.

Phase 2/3 Study in Bipolar Disorder

- A phase 2/3 multicenter, inpatient, double-blind, placebo-controlled study of BHV-7000 for the acute treatment of manic episodes (with or without mixed features) associated with bipolar disorder type I
- Approximately 256 participants will be randomized 1:1 to BHV-7000 75 mg or placebo once daily and treated for up to 3 weeks (**Figure 2**); endpoints are listed in **Table 2**

Figure 2. Phase 2/3 Study of BHV-7000 in Bipolar Disorder



Select Inclusion Criteria	• Aged 18-75 years at time of consent • Voluntarily hospitalized for a current manic episode (YMRS ≥ 20) • Meets *DSM-5* criteria for bipolar disorder type I, with or without mixed features, as confirmed by MINI interview with at least 1 well-defined prior mood episode (in addition to the current episode) in the last 2 years • Episode of mania must not exceed 12 weeks in duration • Able and willing to discontinue all other psychotropic medications during screening
Select Exclusion Criteria	• Rapid cycling, defined as ≥ 6 distinct mood episodes in a year • Confirmed history of schizophrenia, psychotic disorders, dementia, delirium, amnesia, neurodegenerative disease, traumatic brain injury with clinically significant sequelae, seizure disorder, or other neurocognitive disorder

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; MINI, Mini International Neuropsychiatric Interview; QD, once daily; YMRS, Young Mania Rating Scale.

Table 2. Endpoints in Bipolar Disorder

Primary endpoint	• Change in YMRS total score: baseline to day 21
Key secondary endpoints	• Change in CGI-S scale total score: baseline to day 21 • Percentage of participants showing treatment response, defined as ≥ 50% reduction on YMRS total score from baseline to day 21 • Percentage of participants showing treatment remission, defined as total score of ≤ 12 on YMRS total score from baseline to day 21 • Change in YMRS total score from baseline to day 7 • Change in YMRS total score from baseline to day 4 • Change in MADRS score from baseline to day 21

CGI-S, Clinical Global Clinical Impression–Severity; MADRS, Montgomery-Åsberg Depression Rating Scale; YMRS, Young Mania Rating Scale.

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DISCLOSURES: AM, **AT**, **SK**, **DS**, **MA**, **LD**, **MB**, **SD**, **IQ**, and **VC** are employed by and hold stock/stock options in Biohaven Pharmaceuticals.

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