



December 7, 2023

Dear Knopp Member:

I am pleased to provide this update on recent activities at Knopp Biosciences as well as reports with respect to Knopp's former dexamipexole and Kv7 programs, which are now being developed by Areteia Therapeutics and Biohaven, respectively.

Areteia Therapeutics

Areteia this year initiated three clinical trials of dexamipexole in eosinophilic asthma: EXHALE-4, a 24-week FEV₁ study (FEV₁ is a measure of the amount of air a person can expel from the lungs in one second) and two pivotal trials (EXHALE-2 and EXHALE-3) of asthma exacerbations that could support regulatory approval. Initial projections were that EXHALE-4 (the shortest trial of the three) would have top-line readout by the end of Q1 2024.

Unfortunately, enrollment in EXHALE-4, as well as the other two trials, has fallen far short of expectations because of higher-than-expected screen fail rates (the rate at which potential subjects fail to meet the criteria for entrance into a clinical trial). Areteia management developed a revised business plan to greatly expand the number of countries and sites to conduct these three clinical trials, thereby enlarging the pool of potential subjects. The revised plan contemplates a delay of 8-12 months for all three trials and significant additional cash needs.

The investor syndicate led by Bain Capital Life Sciences (the Bain Syndicate) that funded the original \$175 million investment in June 2022 (the First Tranche) agreed to restructure their funding commitment to provide an additional \$100 million starting as soon as this month (the Second Tranche), plus another \$150 million after the EXHALE-4 topline readout, assuming a positive result from that trial (the Third Tranche). This new Second Tranche replaced the \$25 million SAFE offering that was committed to last January but not yet funded.

Unfortunately, Knopp members will not have an opportunity to invest in the Second Tranche or Third Tranche because of the significant minimum funding commitment required, including an obligation fund the Third Tranche at a 1.5x level if certain clinical milestones are met.

Knopp, the other Areteia investors, and Areteia management remain committed to and positive about the prospects for dexamipexole in eosinophilic asthma. However, we will have to wait somewhat longer to obtain clinical results to back that up. Additional information about Areteia is available at <https://areteiatx.com>.

Kv7 Program

Generally speaking, Knopp relies on publicly available information with respect to Biohaven's activities. According to Biohaven's most recent public filing, it intends to initiate Phase 3 trials of BHV-7000 (a former Knopp compound) in focal epilepsy before the end of this year and in bipolar disorder in 2024. It also plans to open an IND for BHV-7010 (another former Knopp compound) in epilepsy and mood disorders in 2024.

Other recent good news from Biohaven relating to the Kv7 program includes:

- Positive data from an electroencephalogram (EEG) biomarker study of BHV-7000 confirmed central nervous system (CNS) activity caused by the compound
- EEG study showed dose-dependent and time-dependent effects on EEG across all brain regions and spectral frequencies
- Successfully completed development of extended-release (ER) formulation of BHV-7000 to enable once-daily dosing in clinical trials; established relative bioavailability of the ER to standard release formulation
- Differentiated safety profile from Phase 1 SAD/MAD study showing favorable CNS adverse event profile compared to other anti-seizure medications

Per Knopp's agreement with Biohaven, Knopp would receive a \$10 million milestone payment upon the opening of an IND in the United States for BHV-7010. Also, full enrollment of the focal epilepsy trial of BHV-7000 would lead to a \$25 million milestone payment to Knopp. That said, it's possible Biohaven will initially open its IND for BHV-7010 outside the U.S. (as it did with BHV-7000), and full enrollment of the focal epilepsy study may not happen until 2025. So, although additional milestone payments may be forthcoming, none are imminent. Additional information about Biohaven is available at <https://www.biohaven.com>.

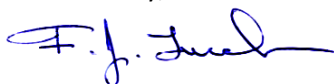
Knopp Biosciences

Knopp's second quarter and third quarter compiled financial statements are available on the Knopp Investor Portal. If you haven't obtained access credentials for the Portal, please reach out to Dave Winklebleck at dave@knoppbio.com.

If you have any questions or concerns about the contents of this letter or otherwise related to Knopp, please feel free to reach out via email to me (fjlucchino@knoppbio.com) or our Vice President, Finance and Investor Relations, Charlie O'Hanlon (charlie@knoppbio.com) or via phone at 412-488-1776.

Happy holidays!

Sincerely,



F.J. Lucchino
President