ELYSIUM
THERAPEUTICS

July 18, 2023

Dear Investor:

We are pleased to provide you with an update on our progress in our programs as well as the financing round that we initiated last fall.

O2P™ Program – hPOC Study

The data from the initial dosing of the first cohort in the O2P human Proof-of-Concept (hPOC) study demonstrated that trypsin inhibition (i.e., oral overdose protection) is viable in human subjects as expected based on preclinical animal models. Further, the extent of trypsin inhibition with ETR028 with its potent appended trypsin inhibitor is stronger than what we observed in preclinical animal studies resulting in reduced opioid delivery efficiency at therapeutic doses. Consequently, we decided to amend the clinical protocol to more thoroughly evaluate ETR029 with its less potent appended trypsin inhibitor, as its lower potency trypsin inhibitor may prove effective in both (i) the release of therapeutic levels of hydrocodone, and (ii) achieving the desired overdose protection profile. We are pleased to report that the FDA approved the revised protocol last month and dosing of the next cohort will begin this week. If this study is successful, O2P hydrocodone would be the first demonstration of oral overdose protection for an immediate-release opioid in humans. We could achieve this milestone by year-end if dosing for the remaining cohorts goes according to plan. Positive data would position O2P hydrocodone for potential Breakthrough Therapy Designation, an FDA process that would expedite its development and approval.

XpiRx™ ("Expiring Pill") Program

As previously reported, we consider the XpiRx program a backup program subject to the results of the O2P hPOC study; thus, we are not currently investing in this program.

SOOPR™ (Synthetic Opioid Overdose Prevention and Rescue) Program

Fentanyl, a highly potent synthetic opioid has flooded U.S. streets and is now found in nearly every illicit drug supply. As a result, there has been a devastating rise in synthetic opioid overdoses. Their high potency and long duration of action frequently requires more than one dose of naloxone (like Narcan®), because it wears off well before fentanyl has been eliminated from the body. Moreover, the discomfort of withdrawal symptoms and short-lived reversal attending Narcan leads many individuals to reuse immediately upon discharge from medical care, increasing the risk of death from a repeat overdose. Sadly, data for the recently approved nalmefene intranasal delivery device, OPVEE™, does not support a longer duration of action needed to combat synthetic opioid (e.g., fentanyl) overdose – especially when taken orally.

Unlike short-acting Narcan, which may require six to 10 doses to safely transport a synthetic opioid overdose victim to the hospital, a single dose of SOOPR is designed not only to rapidly rescue an individual from a fentanyl overdose but will continue to effectively block opioid receptors for 18-24 hours. This reduces risk of re-narcotization, or the return of overdose symptoms, and thus, significantly reduces the likelihood of death or serious brain injury. SOOPR's long duration of action will also (i) prevent same-day re-use of opioids potentially leading to another overdose, and (ii) provide loved ones of individuals suffering from opioid use disorders and first responders with the peace of mind that comes from knowing

they are equipped to save a life and help someone on the road to recovery. Importantly, SOOPR will also provide unmatched protection to the substantial population of individuals who refuse transport or admission to emergency rooms.

We are pleased that we have already demonstrated in vivo proof of concept for duration of action up to 24 hours in animal models. With the additional funding described below, we are moving the SOOPR program forward aggressively to achieve the following goals by 1Q2024:

- Synthesize material for in vivo studies and initial evaluation of delivery devices;
- Complete additional in vivo studies to further support SOOPR's duration of action and rapid onset;
- Identify alternative FDA-approved, easy-to-use delivery devices for our rescue agent; and,
- Meet with the FDA to agree upon the development path for SOOPR.

Financing

Last year, the Board and shareholders authorized an extension of the Series Seed IV round with a goal of raising up to $5M. Thanks largely to the support of existing investors, we completed an initial closing of ~$1.25M in late September 2022. To advance SOOPR to its next value inflection point that could lead to an early-stage deal and to complete the O2P hydrocodone hPOC, another key value inflection point, we needed to continue this round of financing. With shareholder approval to extend the round through June 30, 2023, we are grateful to report that we raised an additional $2.3M, which we expect will be sufficient to complete the O2P hPOC study and the activities outlined in the SOOPR program above. We plan to use these data to pursue potential commercial partnerships as well as non-dilutive grant funding to advance our programs toward the market.

The need for our products has only increased since we founded Elysium, and we are committed to do whatever it takes to advance our programs to market. Just one success from our portfolio could save thousands of lives and generate significant value.

If you have questions, please feel free to contact me.

Thank you and best regards,

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