ELYSIUM
THERAPEUTICS

February 8, 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

We completed the initial dosing of the first cohort in the O2P human Proof-of-Concept (hPOC) study, a Phase 1, randomized, two-part study to evaluate the safety and pharmacokinetics of immediate release oral overdose protected O2P hydrocodone prodrugs (ETR028 and ETR029) in healthy adult subjects. We refer to this study as a human proof-of-concept study as we are not only testing the ability of our technology to deliver known analgesic levels of hydrocodone within the prescribed dose range, but also to evaluate the extent to which our technology provides oral overdose protection – i.e., a meaningful reduction in maximum hydrocodone exposure in overdose scenarios. If successful, O2P hydrocodone will be the first demonstration of oral overdose protection for an immediate-release opioid. These data would position O2P hydrocodone for potential Breakthrough Therapy Designation, an FDA process that would expedite its development and approval.

In the initial cohort, we dosed a total of 24 healthy subjects, and there were no safety issues. Six subjects in four different groups either received 30 mg of ETR028, 30 mg of ETR029, 5 mg of hydrocodone, or 10 mg of hydrocodone. While a single dose level does not a trend make, we are excited about the results which not only showed that the molecular delivery subunit released hydrocodone, but also there was a clear difference in hydrocodone exposures between ETR028 and ETR029 that correlated with the respective potencies of the trypsin inhibitor subunits present in ETR028 and ETR029 responsible for governing exposure of hydrocodone. While we do not yet have sufficient data to definitively reach this conclusion, it does appear that the trypsin inhibition in humans is stronger than what we observed in animals. Consequently, we decided to modify the clinical protocol to evaluate ETR029 more rigorously, 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.

While we saw no safety issues, we did have one subject with one time point where an ETR028 derived metabolite exceeded the levels set by our PK stopping criteria. Importantly, this subject, like all other subjects experienced no safety issues. Consequently, we also amended the protocol to allow more flexibility in the dose escalation of ETR028 and ETR029, alone or in combination, based on the well-established safety of these prodrugs and their respective derived metabolites observed in both IND-enabling animal studies and initial human dosing.

These protocol amendments are currently under review by the FDA. We will continue the study with the next cohort as soon as we obtain FDA approval for the proposed clinical protocol amendments. The Agency indicated that their designated reviewer is actively reviewing our request; thus, while we do not have a commitment on timing from the FDA, we would expect a response by next month.

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.

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THERAPEUTICS

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. The tragic rise in synthetic opioid deaths is clear evidence that existing rescue agents, like Narcan®, are no match for these potent opioids.

In the year ending April 2021, fentanyl overdose claimed the lives of 40,010 Americans ages 18-45—more than car accidents, suicide, COVID-19, and cancer and is now the leading cause of death for this age group. Imagine a Boeing 737 crashing every single day, and you will get a sense of the magnitude of fentanyl fatalities.

Sadly, not enough is being done to protect individuals from the devastation brought on by fentanyl and other more powerful synthetic opioids. Elysium Therapeutics is working to change that.

We interviewed first responders and OUD treatment professionals about what an effective solution should look like. We used their input to guide the design and key attributes of our SOOPR (Synthetic Opioid Overdose Prevention and Rescue) program. Unlike short-acting Narcan, which may require six to 10 doses to safely transport a synthetic opioid overdose victim to the ER, 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 OUD sufferers 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 those 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. However, we need additional funding to advance this program to a value inflection point that may be sufficient to attract a partner to license or acquire our technology. This is the focus of our continued financing efforts.

With the devastating number of deaths claimed by synthetic opioids, the NIH and FDA are calling for stronger, more effective rescue agents. Pharmaceutical companies are waking up to this need as well. Recently, Indivior acquired Opiant, who developed Narcan, for ~$150M upfront, and the potential for an additional ~$50M depending on the success of Opiant's follow-on product (OPNT003). Experts have indicated that our SOOPR program's product profile is far superior to OPNT003, and it is unclear how much better OPNT003 will be compared to Narcan in rescuing individuals from synthetic opioid overdose.

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 are continuing to pitch to new investors to raise up to $3.75M in the existing round. We are grateful to report that we have received indications of interest from a number of angel investors.

For additional closings, we will be seeking shareholder approval to extend the round through June 30, 2023. We are targeting the next close later this quarter, with the final closing scheduled for 2Q 2023.

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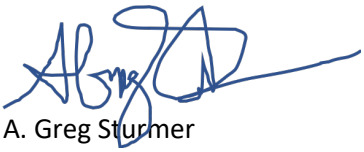
THERAPEUTICS

Since founding Elysium, the opioid crisis has not relented; in fact, it has only gotten worse. The need for our products is more critical than ever before. With your continued support, 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,



A. Greg Sturmer
President and CEO
(650) 464-6175
gsturmer@elysiumrx.com