Elysium Therapeutics Announces Compelling Human Proof-of-Concept Data for its SMART™ Opioid, O2P™ Hydrocodone Prodrug for Acute Pain that Could Disrupt the Industry by Establishing New Standards for Opioid Safety

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Elysium Therapeutics →
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Positive Phase 1 study results achieve a major milestone toward their mission to provide effective acute pain relief while simultaneously mitigating the major risks of existing opioids by protecting against abuse and fatal overdose.

LYONS, Colo., March 5, 2024 /PRNewswire/ -- **Elysium Therapeutics**, an emerging biopharmaceutical company establishing new standards for safety in the opioid industry by developing SMART™ (Safer Medicines Alleviate Risks and Trauma) products, first- and best-in-class medicines to address the limitations and dangers associated with opioids and overdose rescue agents, today announced positive results from a Phase 1, human-proof-of-concept study (O2P-001) investigating the company's proprietary Oral Overdose Protected (O2P™) hydrocodone prodrug for the treatment of moderate-to-severe acute pain. The data

indicate O2P hydrocodone is well-tolerated, delivers therapeutically relevant hydrocodone doses, and provides protection against higher than intended hydrocodone exposures to safeguard against abuse and fatal overdose.

The CDC recognizes the important role of opioids in treating moderate-to-severe acute pain, and Elysium's vision is to establish a new standard for opioid safety in the pharmaceutical industry. Elysium's SMART opioids for pain leverage its O2P technology, a proprietary bifunctional prodrug design, which attenuates the release of the opioid when "supratherapeutic" (more than recommended) doses are ingested. This unique construct is broadly applicable to all commonly-prescribed oral opioid agonists for pain and opioid use disorder.

Greg Sturmer, Co-Founder and CEO of Elysium Therapeutics, stated: "Because non-opioid options are ineffective and existing opioids have no protection against their inherent risks, moderate-to-severe acute pain (e.g., post-operative pain) is not adequately managed in greater than 80% of patients in the US and is associated with increased morbidity, functional and quality-of-life impairment, delayed recovery time, prolonged duration of opioid use, higher healthcare costs, and is predictive of the development of chronic pain.[1] As shown in our human study, our SMART opioids, led by O2P hydrocodone, mitigate the major risks associated with existing prescription opioids without sacrificing their superior analgesic efficacy, especially when compared to currently marketed non-opioid alternatives and those in development."

O2P-001 Phase 1 Trial Overview and Results:

The randomized, open-label, two-part Phase 1 trial enrolled a total of 93 subjects and was designed to evaluate the safety, tolerability, and pharmacokinetics of O2P hydrocodone relative to a hydrocodone comparator following single therapeutic and supratherapeutic oral doses.

Key findings in the O2P human proof-of-concept study include:

- **Safety:** In all treatment periods, O2P hydrocodone was generally well tolerated in all subjects with no serious adverse events reported, even at supratherapeutic doses.
- **Efficacy:** The delivered hydrocodone plasma concentration was consistent with effective management of acute pain and longer duration of action than traditional hydrocodone, meaning a patient would need fewer pills to deliver the same effect. Reducing the number of pills also means lower risk of misuse, abuse, diversion, and fatal overdose.
- **Oral overdose protection:** Following oral administration of supratherapeutic doses, maximum plasma hydrocodone exposures (C_{max}) from O2P hydrocodone were significantly lower compared to traditional hydrocodone. In stark contrast, the hydrocodone comparator produced potentially lethal hydrocodone plasma exposures, while supratherapeutic doses of O2P hydrocodone did not.[2]

Leela Vrishabhendra, M.D., Principal Investigator for the O2P-001 study, commented: "The results from the O2P-001 study indicate that Elysium's O2P technology could yield safer opioids that address the key issues inherent in current opioids that have fueled the opioid crisis, while providing patients with highly effective pain relief."

Commenting on the importance of the study results, Tom Jenkins, Ph.D., Co-Founder and Chief Scientific Officer of Elysium Therapeutics and inventor of trypsin-activated opioid prodrugs and concomitant use of trypsin inhibition to govern opioid exposure, said: "The vast majority (>90%) of acute use opioid abuse is via ingesting multiple intact tablets in excess of the prescribed dose.[3] Results from our O2P hydrocodone Phase 1 study address key issues of existing opioids that too often lead to abuse, addiction, and death by providing meaningful protection against oral overdose; and significantly reducing the number of tablets prescribed."

Sturmer continued: "Given the robust Phase 1 human proof-of-concept data, we plan to meet with the FDA to discuss next steps, finalize our dose form for remaining clinical studies, and seek partners and investors who share our passion to disrupt the pain and opioid use disorder markets with safer medicines that reduce trauma and save lives."

About O2P™ Hydrocodone

Elysium's lead product candidate – oral-overdose protected (O2P) hydrocodone – is a hydrocodone prodrug being developed for the treatment of moderate-to-severe acute pain. Elysium leverages its proprietary bifunctional prodrug technology, containing a trypsin-activated opioid delivery subunit that efficiently releases therapeutic levels of

hydrocodone when exposed to the digestive enzyme trypsin in the lumen of the small intestine, and a trypsin inhibitor subunit that progressively inhibits trypsin, attenuating the release of hydrocodone when supratherapeutic doses are ingested.

About the O2P-001 Study

O2P-001 was a Phase 1, human proof-of-concept, randomized, open-label, two-part study designed to evaluate the safety and pharmacokinetics of O2P hydrocodone in healthy adult subjects. The key objectives of the study were to (i) evaluate the safety, tolerability, and pharmacokinetics of O2P hydrocodone relative to a hydrocodone comparator following single oral doses in healthy adult subjects with naltrexone blockade; and (ii) demonstrate reduced dose-proportional plasma exposures of hydrocodone (i.e., oral overdose protection) of O2P hydrocodone relative to an escalated comparator dose of hydrocodone. A total of 93 subjects were enrolled in the study.

About Elysium Therapeutics

Elysium is an emerging biopharmaceutical company that is establishing new standards of safety in the opioid industry by developing SMART™ (Safer Medicines Alleviate Risks and Trauma) products, first- and best-in-class medicines that address the limitations and dangers associated with opioids and overdose rescue agents to reduce suffering from opioid-use disorder, opioid overdose, and acute pain. Elysium's lead SMART opioid product candidate – oral-overdose protected (O2P™) hydrocodone – is being developed for the treatment of moderate-to-severe acute pain. Elysium is also developing its SMART rescue medicine, SOOPR™ (Synthetic Opioid Overdose Prevention and Reversal), a long-acting opioid antagonist specifically designed to address oral synthetic opioid, including fentanyl, overdose. Tens of thousands of unnecessary overdose deaths each year exemplifies the critical shortcomings of currently available rescue agents, including naloxone and nalmefene. For more information, please visit ***https://www.elysiumrx.com****.*

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