SiteOne Therapeutics Receives NIH Grant to Support the Development of Novel Therapeutics to Treat Ocular Pain

Potential applications in pain associated with ocular surgery, injury, and Dry Eye Syndrome

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BOZEMAN, Montana, Sept. 25, 2018 /PRNewswire/ -- SiteOne Therapeutics, a private biopharmaceutical company advancing novel non-opioid pain therapeutics, today announced the company has been awarded a $1.4 million, two-year, Phase 2 SBIR grant from the National Eye Institute (NEI), a member of the US National Institutes of Health (NIH). The award will be used to initiate IND-enabling studies for SiteOne's Ocular $Na_V1.7$ Program for pain associated with ocular surgery, injury and disease, such as Dry Eye Syndrome. This is the third Phase 2 SBIR grant that SiteOne has received from the NIH, the first having been awarded in September 2014 to support the discovery and development of selective inhibitors of $Na_V1.7$ as therapeutics for acute and chronic pain.

"This new award from NEI represents another important milestone for SiteOne as we continue to advance our portfolio of highly selective $Na_V1.7$ inhibitors for pain," said Stan E. Abel, the company's Chief Executive Officer. "Our lead $Na_V1.7$ program, an intravenous injection for the treatment of postoperative acute pain, is expected to enter clinical testing in 2019. A subcutaneous program will also be advancing into preclinical evaluation later this year. For the ocular program, we anticipate filing an IND in 2020."

The company recently presented preclinical data, including promising tolerability and ocular tissue distribution, for its ocular pain program at the 2018 Association for Research in Vision and Ophthalmology Conference. In this research, administration of a SiteOne selective $Na_V1.7$ inhibitor in a preclinical *in vivo* model resulted in high ocular tissue exposure and tolerability.

"A successful product for ocular pain that can be applied directly to the eye has the potential to be broadly effective in the ~30 million Americans suffering from dry eye regardless of the etiology because it addresses the discomfort rather than the heterogeneous physiologic cause," said John Mulcahy, Ph.D., Vice President of Research at SiteOne. "The analgesic also would complement therapeutics that reduce inflammation or improve tear film, allowing the patient to be comfortable over weeks to months required for these therapies to take effect. Further applications include treatment for postoperative pain following refractive, cataract, and glaucoma surgeries (over 4 million procedures per year in the US) as well as the treatment of ocular injuries (over 2.5 million cases a year in the US)."

About Nav1.7

$Na_V1.7$ is a voltage-gated sodium channel that plays a critical role in the generation and conduction of action potentials in sensory neurons. There has been immense interest in developing selective $Na_V1.7$ channel blockers as novel non-opioid analgesics which may provide pain relief without undesirable effects associated with current opioid therapeutics.

About SiteOne's Ocular Program

The absence of safe and effective strategies for the management of pain associated with various ocular conditions is motivating the development of a novel topical drug suitable for patient self-administration. Conventional local anesthetics, such as proparacaine, inhibit voltage-gated Na+ ion channels (Na_V) and are highly effective for the management of ocular pain in acute, in-office settings. However, these agents are short acting and toxic to the corneal surface, which prevents their use beyond a few administrations. SiteOne has discovered a chemical series of novel, highly selective inhibitors of human $Na_V1.7$, a subtype implicated by human genetics in the transmission of pain including ocular pain. The absence of ocular pain in genetically null $Na_V1.7$ individuals along with the excessive ocular pain in patients with $Na_V1.7$ gain of function strongly suggests that selective inhibition of $Na_V1.7$ is an important new therapeutic approach that can produce significant corneal and ocular pain relief without adverse effects resultant from inhibition of off-target sodium channels involved in vision, smooth muscle function and protective tearing and blinking reflexes. In research studies, ocular administration of $Na_V1.7$ selective inhibitors were well-tolerated and lead to good intraocular exposure.

About SiteOne Therapeutics, Inc.

SiteOne Therapeutics is headquartered in Bozeman, Montana with a research laboratory in the South San Francisco, California. SiteOne is dedicated to developing novel pain therapeutics to safely, effectively and efficiently treat acute and chronic pain without the limitations of existing pain therapies, such as NSAIDs or opioids. The company's therapeutic candidates are highly selective, state-independent small molecule inhibitors of $Na_V1.7$ that block the pore of the channel. Given the critical role $Na_V1.7$ plays in the generation and conduction of pain signals, combined with the urgent need for new, non-opioid pain therapies, SiteOne is focused on advancing its products to serve patients that suffer from moderate to severe pain. For more information, visit SiteOne's web site at www.siteonetherapeutics.com.

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