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Title: Cytogel Pharma, LLC. Announces Presentation at the 8th Annual Pain and Migraine Therapeutics Summit in Boston on September 24, 2014, Novel mu opioid mechanisms for the potent analgesic Cyt-1010 distinguish it from morphine

DARIEN, CT., September 25, 2014

Cytogel Pharma announces the presentation at the 8th Annual Pain and Migraine Therapeutics Summit of a mechanism of action study conducted in the laboratory of Gavril Pasternak, MD, PhD at Memorial Sloan Kettering Cancer Center in New York City. Cyt-1010 is a chemically stabilized and peptidase resistant analog of endomorphin-1, is highly mu-selective, showing very poor affinity for delta and kappa opioid receptors. Despite its mu classification, the pharmacology of Cyt-1010 is clearly dissociable from that of morphine. Cyt-1010 demonstrates potent antinociceptive activity in thermal, inflammatory and neuropathic pain models, by multiple routes of administration, but fails to show reward behavior in a conditioned place preference paradigm and does not produce respiratory depression at analgesic doses. In Phase 1 clinical trial, Cyt-1010 was well tolerated with no serious adverse effects and was active in the cold pressor assay. Yet, it showed no evidence of respiratory depression using oximetry even though its pupillary actions demonstrated penetration of the central nervous system. Recent work suggests that mu opioids can be divided into several classes based upon their activity at different targets generated from the mu opioid receptor gene MOR-1 through alternative splicing, as demonstrated using transgenic knockout mice. Results with selective agents demonstrate that Exon 11 forms mediate analgesia without traditional opioid side effects. Exon 11 MOR-1 knockout mice lose one set of splice variants without altering traditional mu receptor targets. Morphine retains full analgesic activity in these animals without any loss of potency. However, the analgesic actions of Cyt-1010 are significantly lowered, with the ED<sub>50</sub> shifted by well over 2-fold suggesting preferential action of Cyt-1010 through the Exon 11 MOR-1 forms. These results clearly distinguish Cyt-1010 actions from those of morphine at the genetic level and may help explain its unique, advantageous pharmacological profile.

#### About Cytogel Pharma

Cytogel Pharma is a biopharmaceutical company developing promising early-stage programs with significant potential as platform technologies and valuable products. The company's portfolio includes novel analgesic product candidates and broadly useful polymer and hydrogel drug delivery technologies. Cytogel will then license these products to companies for full development and subsequent commercialization. To learn more about Cytogel, please visit [www.cytogelpharma.com](http://www.cytogelpharma.com).