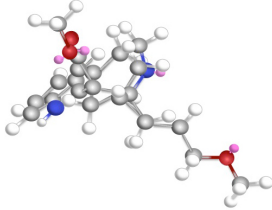


Pipeline

Addiction Medicine 18-MC



Savant's approach is unique in addiction medicine. Current anti-addiction medications are either agonists or antagonists for the addictive substance's primary receptor site of action (such as methadone for heroin addiction, low doses of nicotine for nicotine addiction and naltrexone for opiate dependence) and are themselves often harmful and addictive. These types of receptor strategies do not directly target the underlying addictive mechanism in the brain (extreme fluctuations of dopamine in the mesolimbic system leading to drug craving) that Savant's novel approach targets.

18-MC, a specific $\alpha 3\beta 4$ nicotinic receptor antagonist, is an orally active, synthetic compound that modulates dopamine fluctuations in the mesolimbic system of the brain. Data from animal models demonstrate the efficacy of 18-MC in a broad array of substance addictions, including cocaine, opiate, methamphetamine, nicotine and alcohol, as well as over-eating. The $\alpha 3\beta 4$ nicotinic receptor is a promising anti-addiction drug target. Independent investigators have confirmed that polymorphisms in the $\alpha 5\alpha 3\beta 4$ gene cluster on human chromosome 15 are predictive of heavy smoking and severe nicotine dependence.

Between September 2012 and August 2015, Savant received a \$6.7 million grant from the National Institute on Drug Abuse ("NIDA") to support the preclinical development of 18-MC, resulting in the receipt by Savant of a U.S. IND (Investigational New Drug application) in July 2014. 18-MC began human safety testing in healthy volunteers in late 2014. Having successfully completed the first-in-human clinical studies, 18-MC is scheduled for additional clinical safety studies in 2018.

Market Potential: In November 2016, the U.S. Surgeon General issued Facing Addiction in America – The Surgeon General's Report on Alcohol, Drugs, and Health, which is their first report on addiction since their report on smoking in 1964. In this report, the U.S. Secretary of Health and Human Services, Sylvia Mathews Burwell, noted:

All across the United States, individuals, families, communities, and health care systems are struggling to cope with substance use, misuse, and substance use disorders. Substance misuse and substance use disorders have devastating effects, disrupt the future plans of too many young people, and all too often, end lives prematurely and tragically. Substance misuse is a major public health challenge and a priority for our nation to address.

For 2015, the Substance Abuse and Mental Health Services Administration, or SAMHSA, estimated that over 21.7 million Americans 12 years and older had a chemical substance dependence or abuse problem other than tobacco needing treatment. The total social and healthcare cost to our society of dealing with alcohol and illegal drug abuse is estimated to exceed \$193 billion annually. Fewer than one-in-ten patients receive treatment for their addiction in the U.S., at a cost of one in every four deaths. The combined annual cost of substance use disorders in the U.S. is estimated to exceed \$600 billion – a staggering economic impact.

The opiate abuse problem has grown to epidemic proportions in parts of the U.S. We are exposed to a nearly daily news flow on the problems associated with opiate addiction resulting from heroin use and the abuse of prescription drugs such as OxyContin®, Vicodin®, Percocet®, and Fentanyl®. In 2014, the states with the highest drug overdose death rates included Kentucky, Massachusetts, New Hampshire, New Mexico, Oklahoma, Ohio, Pennsylvania, Tennessee, Utah, West Virginia, and Wyoming - all with death rates between 19 and 35.5 per 100,000 population. To give this context, according to the Centers for Disease Control and Prevention, or CDC, in 2011 the death rate from accidents, including traffic-related, was 42.7 per 100,000 population in the United States. Today, more than 140 people die from an opiate overdose every day in America.

Emerging Neglected Disease Pipeline

Leishmaniasis: Leishmaniasis: Leishmaniasis is spread by the bite from infected sand flies with the estimated 900,000 to 1.6 million new cases per year occurring in over 90 countries, including isolated cases of primary infection in the southern US. US cases come primarily from immigrants from Central and South America, travelers and military personnel exposed in Iraq and Afghanistan. Current treatments for leishmaniasis have significant side effects and limited efficacy. Savant's lead compound in addiction medicine, 18-MC, has demonstrated significant anti-leishmanial activity in disease models, employing a different mechanism of action than that in addiction. Savant is currently pursuing development of 18-MC as an oral treatment for the cutaneous form of the disease in collaboration with a Brazilian

pharmaceutical company. Savant's South American partner began human safety studies of 18-MC in mid-2014.

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