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Dedication | Excellence | Integrity

“Successfully Navigating the Federal Marketplace”

Background:

Drug overdose deaths, driven largely by prescription drug overdoses, are now the leading cause of injury death in the United States – surpassing motor vehicle fatalities. The abuse of and addiction to opioids such as heroin, morphine, and prescription pain relievers is a serious global problem that affects the health, social, and economic welfare of all societies. In 2014, according to the National Institute of Drug Abuse (NIDA), deaths from prescription opioid overdoses were 18,893 and 10,574 from illicit heroin. It is estimated that between 26 and 36 million people abuse opioids worldwide, with an estimated 2.1 million people in the United States suffering from substance use disorders related to prescription opioid pain relievers in 2012 and an estimated 467,000 addicted to heroin. A 2014 report, by the Partnership at Drugfree.org and the New York State Office of Alcoholism and Substance Abuse Services, shows that there are as many as 23.5 million adults in the U.S. who have at one time had issues with their alcohol consumption or drug use.

To address this national pandemic, the U.S. Congress passed S. 524, “The Comprehensive Addiction and Recovery Act” (CARA) in the Senate, March 9th by a vote of 94-1 and in the House of Representatives on May 13th by a vote of 400-5. The Conference Report was passed in the House of Representatives on July 8, 2016 by a vote of 405-7. The legislation addresses prevention and education, law enforcement and treatment, treatment and recovery, incentivizes states, addresses Veteran’s opioid issues and authorizes grants to states to facilitate access to drugs for emergency treatment of opioid overdose including naloxone.

Product Development Concept:

TITLE I Prevention and Education, Section 107 of the CARA Act establishes grant programs to help states provide opioid overdose reversal medication access and education.

Naloxone was patented in 1961 and the drug was approved for opioid overdose by the Food and Drug Administration (FDA) in 1971. Naloxone is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system. Naloxone is available as a generic medication. On November 18, 2015 the Food and Drug Administration (FDA) approved a naloxone nasal spray product by Adapt Pharma and Opiant Pharmaceuticals, Inc. marketed as Narcan. Until this approval, naloxone was only approved in injectable forms, most commonly delivered by syringe or auto-injector.

Law enforcement departments in 28 states now carry naloxone to quickly respond to opioid overdoses, 40 states and District of Columbia have “standing orders” from the states health official for over-the-counter sale of naloxone. Naloxone is used to resuscitate patients from respiratory or mental depression due to opioid overdose, most commonly injected intravenously for fastest action, which usually causes the drug to act within a minute, and lasts up to 45 minutes. It can also be administered via intramuscular, subcutaneous injection or nasal spray.

Naloxone prescription is recommended if a person is on a high dose of opioid (>100 mg of morphine equivalence/day), is prescribed any dose of opioid accompanied by a [benzodiazepine](#), or is suspected or known to use opioids nonmedically. Contributing factors to the current national opioid drug abuse problem include drastic increases in the number of prescriptions written and dispensed, greater social acceptability for using medications for different purposes, and aggressive marketing by pharmaceutical



companies. The number of prescriptions for opioids (like hydrocodone and oxycodone products) have escalated from around 76 million in 1991 to nearly 259 million in 2012.^{1/} The United States accounts for 81% to 100% of the world total for Percocet and Vicodin.

Transdermal delivery (TDD) of naloxone may be effective for opioid overdose resuscitation and/or by opioid dependent individuals to avoid opioid overdosing. Currently there is no prescription drug product approved for sale that utilizes transdermal patch technology in this medium. Patch technology suggests that the active ingredient of naloxone could be delivered through the outer layer of the skin for a period of two hours to two weeks in duration.

Northport's Naloxone Patch Patent Application Accepted-Patent Pending:

Northport Research, Inc. was notified by the United States Patent and Trademark Office (USPTO) on October 27, 2016 of its patent pending for a Transdermal Drug Delivery System (TDDS) to Deliver a Therapeutically Relevant Formulation of Naloxone to Stop or Reverse The Effects of an Opioid Overdose and to Maintain Steady-State Levels of the Drug to Prevent Opioid Overdose Over a Prolonged Duration Extending Several Days.^{2/}

Northport, working with globally recognized researchers/leaders focused on transdermal prodrugs microneedle-enhanced (MN) delivery, and translational research models for public-private partnerships, is exploring alternative permeation enhanced formulations and delivery methodologies for administering naloxone. Transdermal drug delivery offers an advantageous mode of drug administration by eliminating first pass hepatic metabolism and providing sustained drug release for a prolonged period of time. It is painless when compared to needles and therefore offers superior patient compatibility.

Currently, needle-based injection is the most frequently used route to administer protein and peptide drugs like naloxone. Transdermal drug delivery is an attractive alternative to conventional techniques for administration of systemic therapeutics. One challenge in designing transdermal drug delivery systems is to overcome the natural transport barrier of the skin. Chemical formulations offer tremendous potential to enhancing the transport of naloxone drug molecules combined with microneedle-assisted transdermal delivery of opioid antagonists may deliver therapeutically relevant levels of naloxone to prevent death.

Indicators of Opportunity:

Drug abuse involves non-therapeutic use of drugs resulting in physical, mental and social harm to an individual. Morphine is the most frequently abused drug ([Gutstein and Akil, 2001](#)). Tolerance develops from its chronic use and thus user has to increase dose to get euphoric effect. In US, around three million people are opioid dependent among which about 980,000 are long term users ([Raisch et al., 2002](#)).

Naloxone (NLX), is a non-specific, competitive opioid antagonist and is used to reverse opioid induced central nervous system (CNS) and respiratory depression. NLX shows a short biological half life (64 min) ([Ngai et al., 1976](#)), following its intravenous (IV) administration. Owing to extensive first pass metabolism leading to poor bioavailability of about 2%, peroral route is not effective for its delivery. NLX shows a very short duration of therapeutic effect and thus requires frequent administration by IV or intramuscular (IM) routes which are invasive ([Gourlay and Coulthard, 1983](#)).

Transdermal drug delivery (TDD), being non-invasive, offers an improved approach to administration of drugs by maintaining a therapeutic concentration of drug in plasma over a prolonged duration extending to several days ([Cleary, 1993](#)). Development of a TDDS will thus circumvent the current delivery problems associated with NLX.^{3/}

¹ Centers for Disease Control and Prevention, Vital Signs, Prescription Drug Overdoses

² United States Patent and Trademark Office, Confirmation No., 1836, October 27, 2016

³ International Journal of Pharmaceutics 293 (2005) 213–223



An alternative approach to circumvent drawbacks from oral therapy and painful depot injections to treat alcoholism is transdermal delivery. By initially limiting the input of the drug dose directly to the systemic circulation, extensive metabolism in the liver is bypassed, thereby increasing efficacy and decreasing the chance of deleterious side effects. Transdermal drug delivery systems are trouble-free outpatient products, and monthly reoccurring healthcare visits to receive a painful injection can be avoided.^{4/} TDDS applied to opioid dependency can address a significant population of opioid users that are susceptible to opioid overdoses.

The Drug Abuse Warning Network (DAWN) provides nationally representative patient demographic and visit-level information on emergency department (ED) visits resulting from substance misuse or abuse, adverse reactions to drugs taken as prescribed or directed, accidental ingestion of drugs, drug-related suicide attempts, and ED admissions for substance abuse treatment.

In 2011, there were 5.1 million drug-related ED visits. About one half (49 percent, or 2.5 million visits) were attributed to drug misuse or abuse with a nearly equal number (45 percent, or 2.3 million visits) attributed to adverse drug reactions. Among visits involving drug misuse or abuse, 1.4 million visits involved pharmaceuticals, and 1.3 million involved illicit drugs.^{5/}

About Us:

Northport Research, Inc. is an affiliate of Northport Affiliates, LLC, a Department of Veterans Affairs verified Service Disabled Veteran-owned Small Business (SDVOSB) founded in 2012 to provide expertise to Federal government departments and agencies to improve service delivery and program productivity. Northport's subject matter expertise includes Change Management and Organizational Development, Project Management Support, Business Process Reengineering, Continuous Process Improvement, Business Process Management, Training, Transition Studies and Analysis, Strategic Planning and Performance Measurement, Management Analysis, Quality Management, Information and Records Management, and Acquisition Management Support. Employing root cause analysis, process improvements and rigorous tracking and performance measurement, we seek to enhance quality, continuously reduce defects, streamline processes, increase efficiency of operations and processes, eliminate waste and help standardize operations across the enterprise.

Northport's veteran heritage and multi-faceted leadership experience is grounded on an unwavering dedication to excellence and integrity. Northport's principals and key executives have distinguished themselves in demanding leadership positions in the private sector and the Executive and Legislative branches of Government. Northport principals and staff possess a wealth of experience and expertise managing complex requirements within Federal civilian agencies, the Army and the DoD.

⁴ Microneedle-Assisted Transdermal Delivery of Opioid Antagonists for the Treatment of Alcoholism, www.intechopen.com

⁵ Substance Abuse and Mental Health Services Administration (SAMHSA), The Dawn Report

