FENTANYL ABATEMENT DRUG DISCOVERY PROJECT SUMMARY

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BACKGROUND & CONTEXT

The current opioid epidemic is characterized by an alarming number of deaths worldwide. Fentanyl overdose is currently causing the highest increase of drug-related deaths in the U.S. Mortality rates from illicit Fentanyl usage rose by over 174% in many populations by 2020.

During 2021, enough illicit Fentanyl to kill the entire U.S. population was seized by the DEA. An independent review by the Washington Post confirmed this estimate.

Consequently, novel interventions, such as innovative therapeutics for opioid addiction, signify a pressing, unmet need.

GATC Health is an AI company transforming drug development and disease prediction. Our validated and proprietary **Multiomics Advanced Technology™ (MAT)** platform de-risks drug pipelines and accelerates new therapies to treat disease with accuracy, efficiency and speed never achieved in medical science.

GATC Health is currently evaluating **new opioid abatement drug candidates** that have been identified by our novel AI-based end-to-end drug development platform. In the traditional development of pharmaceuticals, thousands of drug candidates and their formulations will fail during the product development process, including late-phase Clinical Trials.

GATC Health's **Multi-omics Advanced Technology™ (MAT)** drug development platform has the unprecedented ability to model individuals' system-wide responses earlier and more thoroughly than our competitors. As a result, GATC can pare the set of candidate drugs down to 1 to 3 likely successful compounds for clinical testing over 3-6 months, instead of 5,000+ compounds over 4 to 6 years. We can therefore save the pharmaceutical industry billions of dollars while accelerating innovation.

GATC Health is testing our novel abatement drug candidates via in-vitro and in-vivo studies to assess the specificity, safety, and toxicity to assure low toxicity overall and safety for use in humans, while increasing the opportunity for success in human Clinical Trials.

METHODOLOGY

Utilizing GATC Health's machine learning algorithms, neural networks, and our AI-based systems, we efficiently generated likely compounds as drugs for addiction abatement. Our AI team programmed the GATC Drug Discovery Platform to exclude candidate drugs that would be addictive to any extent. GATC's initial set of candidates consisted of over 80 potential abatement compounds for opioid addiction treatment. To accomplish this, we developed a library of compounds based on Multi-omic "Big Data" captured from the analysis of autopsy brain tissue of people who were addicted to opioids.

GATC Health iteratively applied the algorithms noted above to discover & validate compounds for opioid abatement in-silico. Of the 80 initial compounds, a total of three compounds were identified as potentially viable candidate opioid abatement drugs for treatment of Opioid Use Disorder (OUD). Our research team then chemically synthesized these compounds for Pre-clinical drug evaluation studies.

CONVENTIONAL DETOXIFICATION PROTOCOLS FOR FENTANYL & OTHER OPIOID USE DISORDERS

Medical Detoxification of patients taking illicit Fentanyl (often mixed with Heroin or other drugs) is typically initiated with Buprenorphine (SUBOXONE) or Methadone (DOLOPHINE) in combination with Naloxone (NARCAN).

Buprenorphine is a competitive, partial opioid activator (agonist) that will bind strongly to the opioid [mu] receptors in the brain, without producing euphoria. While both Buprenorphine and Methadone are both opiates, if higher doses of Buprenorphine or Methadone are used initially, they will rapidly displace Fentanyl (or Heroin, for example) from those receptors, and can cause acute, severe opioid withdrawal syndrome, which can be life-threatening due to overwhelming Noradrenergic stimulation activity in areas of the brain and the cardiopulmonary system.

Johns Hopkins School of Medicine has published a micro-dosing oral protocol that has been utilized successfully to rapidly initiate Buprenorphine therapy in patients with Opioid Use Disorder, without precipitating opioid withdrawal. Some patients may require continued treatment with this drug for some time in order to prevent withdrawal symptoms as Fentanyl and/or other opiates are cleared from the body, due to accumulation of the opiates in body fat.

Naloxone is a pure opioid blocker (antagonist) that is used to rescue patients with opioid overdoses and respiratory arrest.

GATC'S ABATEMENT DRUGS: BETTER OUTCOMES IF STARTED DURING DETOXIFICATION

For patients in the first three Stages of Recovery, treatment strategies are often focused on curbing cravings, prevention of abstinence syndrome (withdrawal) from cessation of opioid use, and preventing relapses, while patients are working to understand the roots of their addiction. Abatement drugs, **such as the novel drugs created by GATC Health with the attributes described below**, if initiated during Medical Detoxification, can further augment the potential for success as addicted patients progress into the Action Stage of Recovery, which itself often requires their best efforts. **GATC's Opioid Use Disorder Abatement medications are non-addictive by design, and also support the foundation of continued recovery through increased neuroplasticity and remodeling of the brain limbic system pathways away from addiction patterns.** With such assistance, we anticipate that patients will report improved satisfaction and self-worth as Recovery progresses.

GATC HYPOTHESIS: ABATEMENT DRUG ATTRIBUTES ESSENTIAL FOR TREATMENT SUCCESS

A. Treatment medications must not themselves pose a risk for drug abuse. As noted previously, GATC's Opioid Use Disorder Abatement medications are non-addictive by design.
B. Treatment compounds must maintain sufficient Dopamine levels in the "addiction and reward center" (nucleus accumbens) of patients' brains to reduce discomfort, but without causing euphoria, thereby incentivizing patients to continue Opiate Use Disorder treatment.
C. These novel medications must promote remodeling of the brain limbic system with shifts away from learned addiction patterns, by increasing addicted brain neuroplasticity.
D. Potential for use in treatment of other addictions, such as alcoholism and nicotine.

Thus, GATC ensures that our Abatement compounds are non-addictive, and promote neuroplasticity so the "brain gets rewired" to remove "addictive thought patterns" while treatment with the Abatement medication and a 12-Step Program or its equivalent continue. These two parts of the treatment plan are synergistic and reinforce each other, for the benefit of the patient in the addiction recovery program.

DRUG CANDIDATE PRE-CLINICAL EVALUATION TESTING PROCEDURES

A. In-vitro testing: All abatement candidate drugs have already fulfilled the safety and efficacy criteria of the EUROFINS primary target safety panels. Ongoing analyses include:

1. Tier 1 safety panels including targets and pathways that are used for early safety evaluation of drug candidates. Compounds are tested in both functional & binding assays, to identify potential issues early in the drug discovery process.
2. Tier 2 safety panels provide the information for drug optimization by performing early identification of off-target interactions and regulatory assessment of chemical safety.
3. Tier 3 safety panels will be run on the final selections of compounds. Analysis of that data allows GATC to select prime candidate drugs, thereby contributing towards the progression to first-in-human Clinical Trials

B. In-vivo testing is already in process: – Animal studies of drug candidates have begun at UC Irvine using 3 groups of Outbred Wistar rats, with each group receiving intraperitoneal injections of a different abatement compound, in controlled studies with Fentanyl-addicted subject rats, to be compared with Control groups of non-addicted subject rats.

1. **Addiction Model:** Subgroups of rats receiving Intravenous self-administration of Fentanyl via Central IV line – are utilized as the animal model of Fentanyl addiction.
2. **Control Model:** Subgroups of rats without self-administration of Fentanyl – instead receiving saline via Central IV line – are used as the model of Non-addiction.
3. Blood samples for target levels of Fentanyl as well as for blood levels of the abatement drugs will be obtained from subject rats at 3 intervals during the study.
4. Preliminary results from in-vivo testing of abatement drugs currently look promising. GATC is awaiting final pre-clinical results for statistical analysis and testing decisions, including advancement to Clinical Trials with a Pharma partner.
5. In December 2022, Congress passed, and the President signed the **FDA Modernization Act 2.0** into law, which amends 21 USC §355(i) to remove the 1938 mandate for pre-clinical testing of new human drugs on non-human animals. Instead, the law now permits FDA to rely on non-clinical tests including in-vitro, in-silico or in-chemico findings, and hence accelerate the onset of human clinical trials.

C. In parallel with in-vitro and in-vivo animal studies, GATC is planning other IND-enabling studies to assess multi-omic response activity and provide insights into the efficiency and pharmacokinetic performance of our abatement drug candidates. Success of such studies will facilitate the IND process to the FDA for pharmacology and toxicology clearances.

CONCLUSIONS

GATC Health's aim is to evaluate new Abatement drug candidates which have been identified by our novel AI-based end-to-end drug development platform. GATC's novel non-addicting abatement medications will maintain sufficient dopamine levels in the addiction and reward centers to reduce discomfort and agitation while also promoting remodeling of the brain limbic system with shifts away from learned addiction patterns, by increasing addicted brain neuroplasticity. As we conclude our Pre-clinical Testing in the first half of 2023, GATC will confirm our understanding of the specificity, safety, and non-toxicity seen during drug discovery, as well as demonstrate the efficacy of the best candidate abatement compounds. This is an essential part of the drug discovery process and will increase opportunities for success in subsequent clinical trials, in which GATC expects the combination of abatement medication plus a 12-Step Program, or its equivalent, to be synergistic in promoting the Recovery of patients from drug addiction.

Opioid Abatement Settlement guidelines include recommendations for allocating a percentage of funds for research and development. GATC Health is open to establishing relationships with states and other municipalities to support their Opioid Abatement goals by accelerating the availability of this significant new abatement tool for their addiction treatment professionals. GATC is also seeking university, non-profit and commercial partnerships within your state for collaborative research, data sharing, clinical trials, and development. Please contact our office at 833-333-GATC (4282) for information.