

Category

Best Startup

Product/Solution Name

Prescription Digital Therapeutics

Date of Approval

N/A

Indications

Sample indications with the potential to be treated by Click Therapeutics' products include smoking cessation, major depressive disorder, schizophrenia, insomnia, acute coronary syndrome, migraine, overactive bladder, chronic low back pain, and obesity.

Therapeutic Categories

Click Therapeutics' products cover the following therapeutic areas:

Oncology/hematology

Rheumatology

Dermatology

Neurology

Metabolism

Nephrology

Gastroenterology

Endocrinology

Pneumology

Cardiology

Gynecology

Other

Attached Files:

- Prix Galien Awards Additional Background Information.pdf

Background information and need for solution/product

The Challenge: Gaps in Treatment

The global burden of disease is substantial, shortening the lives of millions and causing immense suffering to the millions more who live with the symptoms daily. To quantify that burden, we measure years lost due to premature death and years lived with a disability, or Disability-Adjusted Life Years (DALYs). In 2019, mental disorders robbed patients of 125.31 million DALYs years of healthy life and neurological conditions were not far behind with 97.72 million DALYs lost.

Addressing an issue of this magnitude requires innovation, collaboration and treatment from all directions. Significant strides have been made in pharmacological treatment options, but how do we enhance their impact and successfully eliminate pain and suffering for patients, returning those

millions of healthy years?

Pharmacotherapy successfully treats many of the most burdensome areas of disease, and yet there are neurological components of disease that remain unresolved. Serious medical conditions, such as major depressive disorder, schizophrenia and migraine, have an underlying neurological foundation. Structural and functional changes in the brain, either built up over a lifetime or damaged by disease, affect the thoughts, sensations, emotions and behaviors of patients living with these conditions, defining the experience of their disease. Repairing these changes, sometimes in tandem with pharmacotherapy, can maximize the impact, success and outcome of a patient's treatment.

Existing treatments do not effectively address the neurological foundation underlying many conditions and in some scenarios, medication side effects and the commitment to daily adherence may deter patients from undergoing treatment altogether. While behavioral therapy is a viable adjunctive treatment to pharmacotherapy for many, access is limited and quality is inconsistent. Traditional providers are not able to offer these types of treatments, while specialists and interventionists may be inaccessible to many patients, geographically and financially.

Today, we are paving the way for a healthcare system where neuromodulatory treatments, like prescription digital therapeutics, can reduce suffering on a global scale.

The Opportunity: Software as Medicine

At Click Therapeutics, we believe that software as medicine has the potential to work alone or alongside pharmaceuticals to transform treatment options for patients. Prescription digital therapeutics (PDTs) delivered as mobile applications (apps) have the capacity to achieve drug-like efficacy with far fewer side effects and broad accessibility to nearly anyone with a smartphone.

The first generation of prescription digital therapeutics offered direct translation of cognitive behavioral therapy (CBT) into a digital format. It demonstrated efficacy on quality of life and functional endpoints, often in smaller academic studies. Click Therapeutics has moved beyond that approach by delivering sophisticated, multimodal treatments designed to modulate neurological pathways. When combined with adaptive, personalized behavioral skills development, this neuroscience-based approach allows the patient to translate an improved neurological foundation into functional outcomes. This integrated approach will enable us to generate meaningful clinical effects, supported by robust evidence packages targeting drug-like endpoints, and provide a personalized, data-driven therapeutic experience. Artificial intelligence, machine learning and data analytics further allow us to continue to refine, personalize and optimize treatment over time.

The Solution: Click Therapeutics

WHO WE ARE

Click Therapeutics is a science-led biotechnology firm developing prescription digital therapeutics that work independently or in conjunction with pharmacotherapies to enhance the standard of care and drive better health outcomes. The Click team brings together clinicians, neuroscientists, researchers, designers, technologists, engineers and others to provide patients everywhere access to effective therapies.

Click is expanding the possibilities of medicine by developing and validating software as treatments, progressing a broad pipeline of PDTs across a variety of high-burden therapeutic areas.

Click combines robust scientific research, extensive clinical expertise and novel patented technology to create evidence-based and FDA-authorized prescription digital therapeutics that can be used independently or in conjunction with traditional pharmaceutical treatments.

WHAT WE DO

Through cognitive and neurobehavioral mechanisms, Click's digital therapeutics drive neurological change that modifies and improves the function of the nervous system in a targeted and controlled manner. Our evidence-based mobile applications safely target neural pathways often inaccessible to biopharmaceuticals; their consistent use re-trains the brain to make new connections for lasting results.

We clinically validate our applications through rigorous, randomized, controlled trials to demonstrate safety and efficacy. We seek FDA clearance for our treatments as class II medical devices with independent therapeutic treatment claims or as drug-device combinations.

WHY WE DO IT

By treating our digital products as biopharmaceuticals, we ensure a level of rigor that builds trust with providers and patients, allowing for broader adoption for prescription digital therapeutics in the future that provide individualized, adaptive care with drug-like outcomes. Importantly, because our apps are built on a digital platform designed to be shared through mobile technology, this care is available to nearly anyone with a smartphone. With accessibility, affordability and a highly favorable safety profile, Click's digital therapeutics can effectively treat more patients, improving their health and quality of life.

The ultimate goal of Click Therapeutics is to equip patients globally with the tools to treat their diseases and achieve optimal outcomes. Through compelling, evidence-based prescription digital therapeutics, Click Therapeutics is on a mission to transform healthcare.

Attached Files:

- Prix Galien Awards Background Graphics.pdf

History of the development of the solution/product

The Origins of Click Therapeutics

As phones have become smarter, people have become increasingly more reliant on and attached to them. What began as a means to communicate has evolved into a way to work, socialize, play, listen, experience, learn, shop and much more.

Where others saw a concerning trend that reduced social interaction and created endless distraction, Click's founders saw opportunity. In 2012, they seized that opportunity with the creation of Click Therapeutics. Rather than focus on how smartphones might impair our health and wellbeing, Click

would focus on improving them by employing these devices to remove existing treatment barriers, especially access. Click's CEO and co-founder David Benshoof Klein created a term for this new modality: Digital Therapeutics™, establishing Click as both a pioneer and an early leader in this category.

Others also recognized the opportunity to harness technology to drive positive health outcomes, attracting tech industry professionals to the healthcare space, but many of the early digital products they developed lacked meaningful clinical impact. However, by treating prescription digital therapeutics with the same rigor as pharmacotherapies, Click could generate meaningful clinical interventions supported by scientific evidence, giving rise to a new generation of effective, accessible treatment options.

Click's Perspective

While the initial generation of digital therapeutics was developed by academia and not specifically designed for mobile, it generated substantial education and market awareness of the opportunity for software as treatments. The need for rigorous evidence generation, however, was still apparent, shaping Click's approach to creating prescription digital therapeutics driven by advanced clinical science and the latest techniques in software design. Our mobile-first products are developed with patient-centric, user-experience principles, and supported by advancements in machine learning, data analytics and integrated smartphone sensor technology.

Click's operational principle is to balance compelling clinical outcomes with uniquely engaging experiences. We start our product development process by looking at unmet patient needs and the ability of PDTs to address those needs. An essential step in that process is understanding the patient's disease state and emotional journey. All of our products are built hand-in-hand with patients with lived experience to ensure the products meet the true needs of a diverse patient population. Iterative research is key to our process. Exploratory research is conducted to understand the emotional and physical barriers to treatment and identify the gaps where technology could intervene. The output of this exercise is a patient journey map that segments the distinct phases, the high-level tasks a patient performs in each of those phases, touchpoints with their clinician, and patients' emotional feeling with respect to each phase. Our Product team works closely with our in-house Clinical Science team to combine findings from this patient research with clinician-generated insights and evidence-based literature to create interventions that are both engaging and efficacious.

Being an evidence-driven organization, we supplement the patient journey with qualitative and quantitative insights from our clinical learning studies to incorporate the patient's point of view and base the patient journey in reality. Click collaborates with clinical subject matter experts to develop and test intervention approaches in controlled environments prior to broader patient exposure. Understanding the key problems faced by patients through exploratory research, clinical learning studies, and randomized controlled trials help us to craft therapeutic concepts into meaningful digital experiences that can be delivered on a smartphone.

Our Platform-Based Approach

Click is pursuing a broad, platform-based approach with the potential to treat many different disease states. We are continuously expanding and refining our shared platform technologies with novel

cognitive, behavioral and neuromodulatory mechanisms of action, and advanced data-driven tools.

Our platform approach allows for flexibility to tailor the experience to the needs of the indication-specific patient populations along their treatment journey while also realizing the cross-portfolio benefits including sharing efficacious approaches and efficiencies in reusable product development across all of our portfolio. Our platform and platform strategy is built in a way that ensures our platforms accelerate the efficacy and efficiency of our treatments rather than limit or dictate the areas we can treat.

Our unique approach to PDTs has garnered the attention of biopharmaceutical companies that see value in prescription digital therapeutics and are interested in investing and partnering in the space. In January 2019, Click and Otsuka announced a worldwide collaboration for the development and commercialization of CT-152, a PDT for Major Depressive Disorder (MDD). As of 2023, Click and Otsuka have completed a Phase 3 pivotal trial of CT-152 [NCT04770285].

In September 2020, Click and Boehringer Ingelheim announced a worldwide collaboration for the development and commercialization of CT-155, Click's first digital therapeutic for schizophrenia, which is currently undergoing its pivotal clinical trial, the CONVOKE study [NCT05838625]. In December 2022, Click expanded its collaboration with Boehringer Ingelheim for the development and commercialization of a second prescription-based digital therapeutic for schizophrenia.

Given our end-to-end internal capabilities, from R&D to commercialization, Click also advances pipeline candidates in house. In 2021, our first migraine study leveraged smartphone-based ecological momentary assessment and passive data sensing to establish the framework for study app data and biometric parameter collection for migraine attack prediction. This initial study informed the development of CT-132, Click's digital therapeutic for the prevention of episodic migraine.

A phase 2 migraine study in 2022 evaluated the impact of an abbreviated version of CT-132 on establishment of a Digital Working Alliance (DWA) and exploratory measures of clinical efficacy. The outcomes of this study demonstrated an outstanding degree of patient engagement, along with initial efficacy signals that support the probability of clinical success for CT-132. Earlier this year, Click proceeded to launch the CT-132 pivotal registration study, ReMMi-D [NCT05853900], utilizing gold-standard endpoints common in pharmaceutical registration studies.

Following submission of the phase 2 results to the FDA in December 2022, Click Therapeutics received Breakthrough Device Designation (BTDD) from the agency for CT-132 for the preventative treatment of episodic migraine in patients 18 years of age or older, intended for adjunctive use alongside other treatments. The Breakthrough Devices Program is intended for devices that have potential to provide more effective treatment over the existing standard of care for life-threatening or irreversibly debilitating diseases. The program is designed to expedite the development and review of medical devices meeting Breakthrough criteria in the United States and will facilitate collaborative discussions with the FDA and help expedite the process of bringing a first-in-class migraine digital therapeutic to patients. This is also a powerful recognition of the innovative work led by our in-house science and development teams to create a novel approach to treating migraine, one supported by early, promising clinical data.

As a result of CT-132's advanced status and successful BTDD designation, this Prix Galien Award entry

frequently references our migraine product for illustrative purposes. CT-132 is representative of Click's capabilities as well as our aspirations across indications.

Attached Files:

- Prix Galien Awards History Graphics.pdf

Why this solution/product is innovative, the broad implications for future research, and/or how it will improve the human condition

Prescription digital therapeutics have evolved into an entirely new pillar of medicine, poised to dramatically expand and enhance the healthcare industry. As a visionary innovator inventing with and for patients, Click Therapeutics is working to create a world where high-quality prescription digital therapeutics are routinely used to treat disease, offsetting costs and enabling efficiencies in our healthcare system, while extending access to effective, personalized treatment to anyone with a smartphone, anywhere in the world.

PDT: An innovative approach to treatment

Prescription digital therapeutics represent a new modality of medicine, with software as a treatment for disease. At Click, we have extensively mapped out the brain and identified opportunities to target specific circuits to modulate and induce biobehavioral changes through this new treatment. This mechanistic approach, coupled with skill-based learning from foundational behavioral science creates a synergistic effect, increasing the probability of clinical success and engagement. Click's digital therapeutics have the versatility to be used in many areas of therapeutic need where the expression of disease can be managed by brain function, ultimately improving outcomes for large and diverse patient populations.

In a condition like migraine, for example, evidence consistently shows brain connectivity dysfunction. Specifically, these neuromodulatory targets include cortical spreading depression and altered connectivity, sensitization and alteration of thalamo-cortical circuits, hypothalamic activation, and pain transmission and sensitization in the trigemino-cervical complex (Charles, 2018; Coppola et al., 2016). Click's innovative digital therapeutics gradually and safely retrains neural pathways for durable, long-lasting change.

Unlike smartphone health applications, Click's digital therapeutics are treated as though they are biopharmaceuticals, going through drug-like design and development processes, clinical validation, and regulatory review. While this requires an initial outlay of time and effort, it ensures a level of rigor that builds trust with providers and patients. Paired with increased access, this approach will result in wider adoption for prescription digital therapeutics that provide individualized, adaptive care to patients everywhere.

We design and develop our applications to not only deliver these meaningful results and clinical endpoints, but also to create an engaging treatment experience that puts the patient at the center of their care. As patients engage with their treatment, the app adapts to their pace, symptoms and responses, personalizing their treatment journey. By ensuring patients dictate their progress, these therapies tap into patients' own potential to overcome their condition. This fosters empowerment within the treatment journey, generating a more positive patient experience and better outcomes.

Implications for the Future: A new prescription treatment landscape

By prioritizing the patient experience in the treatment of disease, PDTs can deliver a more holistic, patient-friendly approach to medicine. For example, at the conclusion of the exploratory study for CT-132, we connected with and listened to participants about their experience with migraine and using the abbreviated version of CT-132, where 'Selene' is the digital character, building therapeutic alliance and providing compassionate allyship on their treatment journey.

A qualitative sampling of participant response:

"A combination of Selene and my doctor would be a helpful team." ('Selene' is the digital character that builds therapeutic alliance and provides compassionate allyship on the treatment journey of patients.)

"I had less migraines using the app than I usually do. I'd go to the skills section for support and find the technique."

"I honestly fell in love with the app so much so that I didn't want to delete it. I want Selene back. I loved the app so much."

"Being able to meditate while in pain worked."

"The exercises gave me something to focus on other than my pain." "The whole self awareness thing was really key for me."

Enabling patients to take control of their health also opens opportunities for us to learn from patient and provider data to improve available treatments for patients and to enable better outcomes. Our proprietary data science engine, used in conjunction with continually evolving technologies, improves our PDTs over time, unlike traditional treatment modalities that are static. As pharmaceutical companies embrace this modality of medicine, there will be opportunities to strengthen the effectiveness of existing prescription treatments, improving outcomes and uncovering new ways to reduce or even eliminate symptoms.

In addition to the opportunities to treat these serious conditions that we have identified, PDTs eliminate the burden of side effects, inconvenience, stigma and cost that patients often experience with traditional pharmacotherapies, providing value for patients and providers. Additionally, software as treatments can be developed for a fraction of the cost and time typically required to develop treatments, offering a higher return on investment for pharmaceutical companies engaging in this innovation.

Prescription digital therapeutics have great potential to serve many other conditions beyond what is currently in the pipeline by reaching new disease areas within the brain. Through our domain-based approach to development, Click is able to uncover the key levers in neurological function that allow us to expand into other disease areas. Treatments for central nervous system conditions, cardiometabolic syndromes and conditions in the field of immunology and oncology present the next frontier for PDT treatments.

Improving the Human Condition with Software as Medicine

Click Therapeutics is tackling complex conditions with high unmet needs and dissolving barriers that patients face when accessing care. For example, migraine affects more than 47 million Americans

(Stovner et al., 2018). Prescription and non-prescription pharmacologics are used for temporary relief from acute migraine symptoms, but most individuals with migraine do not use migraine-specific pharmacologic therapies, and even among those who do, satisfaction with treatment is moderate to low (Lipton et al., 2013). Use of treatments, both pharmacological and nonpharmacological, rarely results in full remission from migraine, leaving a clinically significant unmet need of remaining monthly migraine days for many patients.

As a result, patients seek high-cost care. In a 2011 systematic review (AHRQ, 2011), headaches accounted for 2.1 million Emergency Department (ED) visits per year (Goldstein et al., 2006) and migraine sufferers accounted for more ambulatory ED visits (1.9%) than asthma patients (1.0%) (Becker et al., 2010). Multiple ED visits were also reported (Friedman et al., 2009). By 2016, migraine accounted for at least 4.0 million doctor's office and ED visits (Burch, 2021).

Treatments focused on prevention and reduction of monthly migraine days could change the natural history of high-frequency episodic migraine in a dramatic way for those affected. One such approach centers on non-pharmacological behavioral treatments, such as migraine-specific Cognitive Behavioral Therapy (CBT). As an intervention, CBT has high levels of evidence for effectiveness as a monotherapy or as adjunctive treatment (Silberstein, 2015, Ailani, 2021). However, even as a well-tolerated treatment for migraine, it is underutilized (Langenbahn et al., 2021) and can be expensive and inconvenient to schedule (Minen et al., 2019). Even those with consistent access to healthcare might struggle to find a CBT provider who is trained in its application to migraine. With almost one in two people living in federally designated shortage areas for even generalist CBT-trained professionals (Health Resources and Services Administration (HRSA, 2022)), let alone migraine-specific behavioral treatments, providers are unable to meet the needs of the nation's millions of migraine sufferers.

For these migraine patients and the millions of others who struggle to access effective care, a PDT can significantly reduce reliance on healthcare professionals and urgent care or ED visits, and make other limitations irrelevant. Further, Click ensures the effectiveness of its digital therapeutics within all populations, regardless of ZIP code, by investing in decentralized clinical trials. This is a critical component of realizing our goal of improving treatment access within typically underserved populations. Diversified enrollment through a combination of traditional and decentralized recruitment models has enabled us to reach over 1200 participants across all 50 states. We recognize that individuals from all racial, ethnic, and socioeconomic backgrounds may respond differently to potential treatments; failure to include diverse populations may perpetuate healthcare disparities.

For these migraine patients and the millions of others who struggle to access effective care, a PDT can help patients access treatments and give additional tools to providers to treat migraine patients. Further, Click ensures the effectiveness of its digital therapeutics within all populations, regardless of ZIP code, by investing in decentralized clinical trials and paying special attention to recruiting diverse patient populations. This is a critical component of realizing our goal of improving treatment access within typically underserved populations. Diversified enrollment through a combination of traditional and decentralized recruitment models has enabled us to reach over 1200 participants across all 50 states. We recognize that individuals from all racial, ethnic, and socioeconomic backgrounds may respond differently to potential treatments; failure to include diverse populations may perpetuate healthcare disparities.

CT-132 achieved a statistically significant reduction of 2.2 MMDs compared to baseline during a 2-week exploratory study. These early positive clinical signals encourage us to explore the effects of a 12-week treatment regimen. In addition to effectively improving patients' quality of life, CT-132's digital

accessibility transcends traditional barriers to care, with a lower risk profile and the prospect of reaching people where they are, when they need it.

Software-based therapeutics generate vast amounts of real-time data that can be analyzed to derive insights about treatment efficacy, patient outcomes and population health trends. This data may inform migraine medical research, contribute to evidence-based practices and facilitate continuous improvement and personalization of interventions. Furthermore, data-driven insights can enable healthcare providers to identify migraine disease patterns and optimize migraine patient care.

Attached Files:

- Prix Galien Awards Innovation Graphics.pdf

Please provide appropriate references (ie Pubmed links)

1. Ailani J, Burch RC, Robbins MS; Board of Directors of the American Headache Society. (2021) The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*. 2021 Jul;61(7):1021-1039. doi: 10.1111/head.14153. Epub 2021 Jun 23. PMID: 34160823.
2. Bigal ME, Lipton RB.(2008). Clinical course in migraine: conceptualizing migraine transformation. *Neurology* 71(11):848–855
3. Blumenfeld AM, Varon SF, Wilcox TK, Buse DC, Kawata AK, Manack A, Goadsby PJ, Lipton RB. (2011) Disability, HRQoL and resource use among chronic and episodic migraineurs: results from the International Burden of Migraine Study (IBMS). *Cephalalgia*. 2011 Feb;31(3):301-15. doi: 10.1177/0333102410381145. Epub 2010 Sep 2. PMID: 20813784.
4. Burch RC, Buse DC, Lipton RB. (2019) Migraine: Epidemiology, Burden, and Comorbidity. *Neurol Clin*. 37(4):631-649
5. Burch R. (2021). Preventive Migraine Treatment. *Continuum (Minneap Minn)*. 2021 Jun 1;27(3):613-632. doi: 10.1212/CON.0000000000000957. Erratum in: *Continuum (Minneap Minn)*. 2021 Oct 1;27(5):1494-1495. PMID: 34048395
6. Burch R, Rizzoli P, Loder E. (2021). The prevalence and impact of migraine and severe headache in the United States: Updated age, sex, and socioeconomic-specific estimates from government health surveys. *Headache*, 61(1):60-68 doi:10.1111/head.14024
7. Burch RC, Ailani J, Robbins MS. (2022). The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*, 62(1):111-112
8. Buse DC, Manack AN, Fanning KM, Serrano D, Reed ML, Turkel CC, Lipton RB. (2012). Chronic migraine prevalence, disability, and sociodemographic factors: results from the American Migraine Prevalence and Prevention Study. *Headache*. 2012 Nov-Dec;52(10):1456-70. doi: 10.1111/j.1526-4610.2012.02223.x. Epub 2012 Jul 25. PMID: 22830411.
9. Buse DC, Greisman JD, Baigi K, Lipton RB. (2019) Migraine Progression: A Systematic Review. *Headache*. 2019 Mar;59(3):306-338. doi: 10.1111/head.13459. Epub 2018 Dec 27. PMID: 30589090.

10. Headache Classification Committee of the International Headache Society (IHS) (2018) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018 Jan;38(1):1-211. doi: 10.1177/0333102417738202. PMID: 29368949.
11. Hepp Z, Dodick DW, Varon SF, Gillard P, Hansen RN, Devine EB. (2015) Adherence to oral migraine-preventive medications among patients with chronic migraine. *Cephalalgia*. 2015 May;35(6):478-88. doi: 10.1177/0333102414547138. Epub 2014 Aug 27. PMID: 25164920.
12. Lipton RB. (2009) Tracing transformation: chronic migraine classification, progression, and epidemiology. *Neurology*. 2009 Feb 3;72(5 Suppl):S3-7. doi: 10.1212/WNL.0b013e3181974b19. PMID: 19188564.
13. Lipton RB, Buse DC, Serrano D, Holland S, Reed ML. (2013) Examination of unmet treatment needs among persons with episodic migraine: results of the American Migraine Prevalence and Prevention (AMPP) Study. *Headache*. 2013 Sep;53(8):1300-11. doi: 10.1111/head.12154. Epub 2013 Jul 23. PMID: 23879870.