Category

Best Startup

Product/Solution Name

GLX® Signature platform

Date of Approval

N/A

Indications

Multiple Sclerosis
Alzheimer's Disease
Major Depressive Disorder
Atherosclerosis

Therapeutic Categories

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Attached Files:

- GLX Analytix Depth Deck for Galien.pdf
- GLX Analytix Galien_Submission.pdf

Background information and need for solution/product

GLX is a venture backed Danish company pioneering a game-changing early diagnostics and monitoring platform that currently identifies ten different autoimmune, cardiovascular, psychiatric and neurodegenerative diseases with ROC AUCs between 0.80-0.90 through groundbreaking work on the Glycocalyx (GLX). Engaged in partnering dialogues with Roche, Abbott, Beckman Coulter, Amgen, Lundbeck, and Novo Nordisk, and powered by blood samples from MGH, Stanford, Johns Hopkins, Barrow Institute, Tisch, Texas Med, Copenhagen University Hospital and more, the GLX Signature platform will change accessibility, affordability and early identification of hard-to-manage chronic diseases.

Supporting our platform is the creation of the world’s first GLX-focused antibody library, fully owned by us. The GLX-library allows us to ensure top-tier quality and performance of our platform and control our cost-of-goods, alleviating the need for third-party licensing contracts. The library spans all our GLX analytes and we are currently in the final phase of development, ensuring they meet CLSI’s stringent fit-for-purpose criteria.

The GLX Signature platform will enable breakthrough device designation with the FDA, our first clinical product in 2024 as laboratory developed test (LDT) at Cedars Sinai Hospital in Los Angele, and is already active servicing research-use only customers in both pharma and academia.

Chronic diseases are on the rise. The promise of precision medicine, getting “the right drug to the right

person at the right time", has come to fruition, proven its value, and changed lives forever in cancer. 'Get it early' is a known adage in the detection and treatment of most cancers. Patients are segmented based on biomarkers, drugs are designed for each segment and outcomes are drastically increased with early detection, redoubling efforts to screen as early as possible.

The promise of precision medicine for early diagnosis and management of other chronic diseases, however, remains largely unfulfilled. 'Getting it early' is rarely uttered, in part, due to a lack of quality biomarkers. Patients are left in the dark when it comes to diagnosis and monitoring of their condition. Current standard of care arrives too late, after damage has occurred to the body, and treatments begin later, with less chance to succeed.

Our solution is hidden in a large, seaweed-like forest on the blood vessel wall. After almost 10 years of research and a gradual eureka of sorts, we discovered that this cardiovascular forest, called the endothelial glycocalyx (GLX), is released into the blood in response to inflammation and disease. At GLX Analytix, we pluck out this distress signal and reassemble it with machine learning, producing a fingerprint we call the GLX Signature. Since the GLX is the first interaction point between the blood and an organ of the body, the GLX Signature can provide early, upstream information on disease activity. Moreover, it is most dense in the heart and brain and is an active and integral part of the blood-brain barrier (BBB).

For example, in Multiple Sclerosis (MS), an autoimmune disease of the brain, the immune system travels through the blood and enters the brain, causing harm. A person experiences symptoms and receives an MRI. At this point, they don't know if they'll have attacks or flares for the rest of their life or progress to a wheelchair. The MRI only follows damage after damage has occurred in the brain, similar to a more recent development, a blood test for neurofilament light chain (NfL), a protein that is ejected by damaged and dying neurons. These biomarkers are downstream of damage to the brain, after the damage has taken hold.

Since our GLX Signature reflects early disease activity, before damage has occurred in the brain, it can monitor for incoming flares and for effectiveness of a treatment. Indeed, in experimental MS, we showed that GLX increased in the blood 2-4 days before entering the spinal cord and causing harm and in the clinic, the GLX Signature could differentiate MS versus healthy controls with a sensitivity of 95% and specificity of 83% (n=23 in each group), compared to 80% and 45%, respectively for NfL (e.g. Quanterix). Preliminary analyses from our recent scale-up / validation study, a 500+ clinical sample MS flare-detection cohort, has steeled our confidence that the GLX Signature is poised to be a strong player in caring for MS, creating value for patients, clinicians, drug developers and payers.

MS was the first use case for the GLX Signature but that was only the beginning.

Alzheimer's Disease (AD) is a devastating neurodegenerative disease involving the brain, the vasculature, and inflammation. Studies have shown considerable damage to the BBB, the interface between blood and the brain, and loss of blood vessel health is one of the most consequential contributors to dementia. Indeed, cognitive decline advances more quickly and severely in AD patients with vascular pathology and these patients account for 50% of all dementia forms. In a recently published 30-year study, vascular pathology was the earliest and strongest predictor of AD. And yet, an AD diagnosis can take up to 3 years to diagnose after symptom debut. Late diagnosis of AD delays medical intervention and enrolment in experimental trials. Current blood-based biomarkers for AD

diagnosis such as NfL (e.g. Quanterix) and amyloid-beta (e.g. C2N Diagnostics) perform with ROC AUCs of 0.75 and 0.81 respectively. In our first clinical analyses, from a clinical trial in late-stage AD with GLP-1 analogue treatment (N=38), the GLX Signature platform mapped on to amyloid plaque load, cognitive decline, and cerebral metabolic rate and had a ROC AUC of 0.87 versus a healthy control group (N=20). The GLX Signature platform could revolutionize AD diagnosis, and enabling earlier intervention, and supporting drug developers to evaluate the effect of treatments earlier. The data from our scale-up / validation study with 150 AD/MCI versus 150 controls is currently being analyzed.

Mental health disorders are diagnosed through semi-structured, subjective criteria, resulting in a large heterogeneity across different diagnostic categories. Treatments are often ineffective, leaving patients, clinicians and payers at a loss. A blood-based diagnostic marker would represent a major leap forward in relation to early diagnostic precision, relieving the stigma of a diagnosis and finding the right treatment. There is no current blood test for mental disorders such as schizophrenia and Major Depressive Disorder (MDD). The GLX Signature was able to separate drug-naïve, first-episode schizophrenia patients from controls (N=49, 48) with a ROC AUC of 0.87 and our preliminary analyses from a MDD cohort (N=75) suggests a similar or higher performance. In contrast, brain-derived neurotrophic factor, often cited as an active player in MDD, has a discriminatory power of 0.71. Our follow-up with the MDD patients in 6 months will determine our power to detect treatment response and we are processing a treatment-resistant depression cohort in Q3 aimed at flagging the most resistant to current drug therapy early on.

Finally, in another example of the vast potential for the GLX Signature platform, the current standard of care in atherosclerosis involves a CT scan of the heart, in search of calcified plaques. However, a calcified plaque is a late stage manifestation of the disease. Calcium CT is blind to earlier stages such as fibrolipid plaque development and these plaques are the target of current treatment modalities, the cholesterol-lowering drugs. Since the GLX Signature platform enables data-gathering from the blood vessel wall, we are hopeful that we can detect disease, progression and treatment response earlier, before calcification, without ionizing radiation, and long wait-times. Calcium CT scans predict future, major cardiovascular events within 5 years at a ROC AUC of 0.72-0.81 and are not able to discern treatment responders from non-responders in current drugs. We have recently begun a large-scale investigation into improving upon this standard of care with an undisclosed partner.

Armed with the GLX Signature, our GLX library and patent protection, we aim to disrupt the healthcare industry broadly, through patient-centric solutions and a new tool for drug development.

We envision a future where patients are diagnosed earlier, empowered to monitor themselves and treatment plans are optimized, realizing the promise of personalized medicine for chronic diseases. We aim to improve lives all over the world.

Attached Files:

- GLX Analytix Galien_Submission.pdf

History of the development of the solution/product

Modern imaging techniques in the 2010s revealed that an often forgotten structure on the blood vessel wall, the GLX, was 10-100x larger than previously thought. We discovered that the GLX is cleaved off by immune cells in specific patterns before they invade an organ, causing harm. Digging deeper, we concluded that, since the GLX was the first interaction between the blood and the organs of the

body, signals from the GLX could be game-changing for early diagnosis and monitoring of a wide range of chronic diseases. This breadth of possibility led to the filing of two patents, our first investment (~700k USD) and the official launch of the company. From the beginning, we remained agnostic to the 'pieces' of the GLX that would prove most value in a test. We built a custom immunoassay that plucks out all 12 components from a blood sample and a machine learning pipeline to reassemble them, thus, establishing the GLX Signature platform.

We applied the GLX Signature platform to discovery cohorts of fifteen different autoimmune, cardiovascular, psychiatric and neurodegenerative diseases and ten met our 'go' criteria: a ROC AUC of 0.80 with 80% sensitivity / 80% specificity against a matched healthy group (cohort sizes ranged form 20-50 disease and 20-50 healthy samples). Some ROC AUCs were +0.90.

In the same year, we received a number of grants (~300k USD) and were awarded Startup of the Year at the Roche's Future of Healthcare event.

On the back of this success, we raised a strong, venture-backed seed investment (1.7m USD) from an international syndicate involving Denmark's largest VC, and led by Silicon Valley-based Digital Dx Ventures (Michele Colucci) and took our next step.

We calibrated the size and character of our validation cohorts with inputs from potential strategic partners such as Roche, Sanofi, Lundbeck, and Novo Nordisk and potential future target firms for our Series A and acquired 150-300 samples for our beachhead indications (MS, AD, MDD) from biorepositories from 10 top institutions across the US (e.g. MGH, Stanford, John Hopkins, Barrow Institute, Tisch, Texas Med, Ohio State and more) and at Copenhagen University Hospital in Denmark. Focus was made on gender-matching to the real-world prevalence (70% female) for healthy and disease cohorts and mirroring the ethnic diversity of the US, where we will launch our first product. With ethnically-diverse, multi-site collections, from the prevalence of the population we aim to serve, our strategic decisions are based on a strong approximation of the real-world.

We are currently analyzing the data. Each indication that meets the 'go' criteria for commercialization has its own commercialization plan, inclusive of intended use, distinct market analyses, regulatory and reimbursement strategies. 'Go' criteria was established based for each 'intended use' through competitive analyses of competing solutions and targeted Voice-Of-The-Customer interviews with top clinicians at Harvard, Cedars Sinai, Barrow Institute and the Copenhagen University Hospital designed to extract the performance criteria they would want in a test.

We will target one indication at a time, starting with a filing for FDA breakthrough device designation, drafted by our regulatory advisor former chief of product review for medical devices at the FDA, Elliot Cowan and with a breakthrough device designation in hand, we will use our sprint discussions (or qSub dialogue if the breakthrough is not awarded) to hammer out the pivotal trial the FDA would like to see for IVD approval.

As we gear up for a pivotal trial, we will launch a Laboratory-Developed Test (LDT) at Cedars Sinai in Los Angeles at their new CLIA-certified lab, the Precision Biomarker Laboratory in late 2024. Susan Mockus, executive director has submitted a letter of support for this award submission, which was distilled into a testimonial at the tail end of the attached deck, indicating their passion for our GLX Signature offering. This milestone, on track to be achieved in 2024, would be achieved 2 years faster than the

median time-to-market for a blood test in the past. Top-tier clinicians at the aforementioned institutions are supporting our path and interested in seeing the GLX Signature platform on their physician-portal menus.

The vast network of our diagnostics-focused VC and Chair, Michele Colucci, as well as our participation as an industrial partner to the Harvard / Wyss Institute Diagnostics Accelerator has brought top-tier diagnostics and go-to-market experts into our orbit (see team slides in deck), in support of our transition from science to commercial, including Jerry Lanchbury of Myriad Genetics and Gisela Paulsen formerly Senior VP at Roche and Richard Frank former CMO of Siemens Healthineers.

On the financial side, we recruited a top-tier Silicon Valley CFO, Nancy Hargreaves, who is hard at work validating our market assumptions and strategy through her experienced lens. With the COGS under our control via the GLX antibody library and the piggybacking strategy at Cedars, we are targeting a price-point of ~400 USD. For comparison, C2N Diagnostics' PreClivityAD amyloid-beta test is ~1250 USD and Scipher Medicine's PrismRA test, which aims to detect treatment non-responders in rheumatoid arthritis is +2000 USD. Both of these tests use expensive, slow, bulky, and specialized machinery, whereas our solution, utilizing immunoassay chemistry, is the tried-and-true workhorse of a clinical chemistry lab. We are currently in dialogues with Roche, Beckman Coulter, Abbott and Thermo Fisher to discuss partnering our GLX Signature platform with their existing machinery, which in the mid-term is part our strategy to protect our first-mover status, in addition to the patents filed and trade secrets produced (GLX-antibodies). Slotting into existing infrastructure will - with the right partnership - accelerate our market capture and entrench us as the 'go-to' in GLX testing.

Finally, the GLX Signature platform also supports a fee-for-service model for pharmaceutical companies and academics for research-use only. We have been receiving paid jobs since 2021 and are in deals or dialogues with a number of both large and small biotech companies (e.g. Amgen, Biogen, Novo Nordisk, Janssen, Roche, Kariya Pharma, Reservoir Neuroscience) interested in our offering for their indication of interest. A number of these clients and prospective clients have entered a testimonial for this submission at the tail end of the attached deck. We have not yet invested sales and marketing into the GLX Signature platform as a service since we are focused on bringing solutions to patients. However, the traction we have, through word-of-mouth, is indicative of the thirst for new, upstream and dynamic biomarkers of disease. As this service gains more traction, we will invest in the resources needed to meet the demand and/or partner with clinical services laboratories such as Q2 solutions, who have recently expressed interest.

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

The GLX Signature platform is a new class of biomarker that can have an enormous ripple effect across the healthcare industry, broadly.

Our platform is already enabling a new perspective on the importance of the vasculature in disease, offering a new window into inflammation and organ-barrier function, including the elusive BBB. This new tool will embolden new therapeutics and significantly derisk drug development in chronic diseases. The interest, traction and early revenue that we have from clinicians and biotech companies supports the lack of upstream biomarkers currently available and the thirst for our solution.

At our core we are a differentiator: we are an upstream and dynamic biomarker of disease activity.

Alternative technologies are detecting damage very late in the process, measuring dying or dead tissue, such as NfL, whereas, on the other end of the spectrum, other technologies, like DNA sequencing are too static, locked inside your DNA, unable to say if and when a disease will develop. Mass spectrometry-based tools, so-called 'omics' solutions, are complex readouts, hard-to-scale and are often measuring so many analytes that error propagates leading to high run-to-run variability that struggles to meet fit-for-purpose in the real-world. These platforms, although powerful for early stage research, often remain in the 'discovery' phase, providing a service to the research-use only market.

At GLX Analytix, we are laser-focused on bringing our solutions to patients with large unmet needs across a number of debilitating and life-threatening chronic diseases. We are leveraging all the support we can to sprint to our goals, including the breakthrough device designation at the FDA, where we have our first submission in preparation. For reimbursement, we have been in dialogue with Optum from the private payers perspective and CMS for the public for over a year and have initiated the cost-effectiveness analyses that have been requested from us. After calibrating this analysis, we will propose to pilot our offering in Optum's 6-month ManageCare program and with CMS, we propose to align our pivotal FDA trial with the outcomes they desire and conduct the proper trial in tandem.

In the near-term, we foresee a time where the GLX Signature platform is readily available in clinics across the US, slotting into existing infrastructure. In the mid-term, we will leverage the unique, specialty dataset that we will have gathered for improving the test's performance, detecting disease earlier, and supporting clinical trials and the infrastructure we have built for launching new products for the other diseases in our pipeline. In the long-term, we envision a miniaturized at-home test available for self-monitoring and a pairing of our test with a therapeutic that reduces a diagnosis in a chronic disease to a manageable condition.

Fifty-two percent of the US population has one chronic disease, 27% suffer from two or more. More than 2 trillion dollars are spent on managing chronic diseases worldwide and 36 million succumb to their illness. We are changing that paradigm through earliest identification, when treatment can have the greatest impact on lives and our healthcare systems. A precision medicine future for chronic diseases is emerging: we are at the forefront of the biomarker-based revolution.

Please provide appropriate references (ie Pubmed links)

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- Testimonials GLX.pdf