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PRIX GALIEN USA

PRODUCT / SOLUTION

Company Name: WhiteLab Genomics
Product/Solution: Artificial Intelligence based platform for the discovery and design of new genomic medicines (GM)
Date of Approval (If FDA/EMA approved): N/A
Sub-Categories (Digital Health /Medtech / Biotech): Digital Health and Biotech
Categories: All therapeutic areas subject to Genomic Medicine development. It includes notably rare diseases, neuroscience, oncology and ophtalmology.

BACKGROUND

Genomic Medicines (GM) show significant promise but need substantial innovation to unlock full potential for patients.

The NIH reports that nearly 7,000 rare diseases affect more than 25 million Americans. Approximately 80% of rare diseases are caused by a single-gene defect, and about half of all rare diseases affect children. Since most rare diseases have no approved therapies, there is a significant unmet need for effective treatments. GM represent a novel class of biotherapies that utilize DNA and RNA as therapeutic agents. It holds the potential to cure patients suffering from various type of diseases, from neurological disorders, cardiac conditions, cancers, and rare diseases. According to the American Society of Gene & Cell Therapy, 3,726 therapies are reported in development from preclinical to pre-registration in 2022. Gene therapies (GT) account for 55% of this pipeline, including genetically modified therapies such as CAR T therapies. Recent advancements have further expanded the field, with two approvals in late 2022: Hemgenix for hemophilia B and Adstiladrin for bladder cancer, both in the US. Despite this huge potential, only 24 GT have been approved to date in the US. Developers faces significant challenges, including lengthy development times exceeding 15 years (versus 10 for small molecules), high risk of failure and product development costs surpassing $1.5 billion per drug (versus $1 billion for small molecules). Also, GT are often requiring viral vectors used as a cargo to deliver a specific therapeutic sequence to its target. This induces major challenges related to viral vectors viability, limited tropism for a specific cellular target, immunogenicity reducing efficacy and inducing toxicity. Consequently, it contributes to the expensive nature of these therapies. Zolgensma, a one-time-only gene therapy using Adeno Associated Virus 9 (AAV9-SMN1) for Spinal Muscular Atrophy is costing approximately $2 million per patient raising ethical consideration for treatment access around the world.

How AI can accelerate R&D for cell and gene therapies

Generative artificial intelligence (AI) is on the spotlight with ChatGPT impressive ability to generate human-like text. The impact of AI on traditional drug discovery is in its early stages, but we have already seen that when layered into a traditional process, AI-enabled capabilities can

substantially speed up, improve individual steps, and reduce the costs of running expensive experiments. In early 2020, Exscientia announced the first-ever AI-designed drug molecule to enter human clinical trials. In July 2021, AlphaFold, predicted the protein structures for 330,000 proteins, including all 20,000 proteins in the human genome. The AlphaFold Protein Structure Database has since expanded to include over 200 million proteins, covering nearly all cataloged proteins known. With the promise of lower costs and shorter development timelines, AI-enabled drug discovery holds massive potential to increase the accessibility of drugs and to treat presently incurable conditions. But there is significant untapped opportunity in the industry to scale AI in Genomic Medicine as biotechnology companies enabled by machine learning (ML) are still rare. In this context, David Del Bourgo, MBA, and Julien Cottineau, Ph.D., decided to create WhiteLab Genomics in 2019 to unleash the potential of GM with AI.

DEVELOPMENT & CLINICAL OR PRECLINICAL EVIDENCE

Deeptech startup based in Paris and Boston with 25+ employees including 10+ PhD

This past decade has seen a phenomenal growth of the computational power, in-silico modelling and data-driven approaches emerged as indispensable methods for solving complex biological problems. WhiteLab has constituted a team of world-class specialists in AI and biology divided into four group: computational biology, structural biology, data science and biology committed to tackle challenges faced by biopharmaceutical companies in research and early development phases. WLG spent 3 years and significant R&D efforts years to aggregate, curate and structure large public databases so far untapped with the end gold to foster and de-risk research and development for CGT. Our development includes state of the AI/ML technologies, using Natural Language Processing, Knowledge Graph Intelligence with specific Ontologies and Multi-Omics databases. Notably, we have developed a proprietary biomarker cellular atlas to identify new biomarkers with specific expression for a particular tissue or cell type.

- **First year** was mainly dedicated to identifying and access relevant sources of data: Text Based Data (Publications, Clinical Trials, Patents, Regulatory), Biological Data (Omics Tissue/Organs/Cells, Vectors, Plasmid), Experimental Data (Expression in tissues / organs /cells, Genotoxicity, Vector production)
- **Second year** was focused on the development of knowledge AI for data Curation and ontologies, development of our technological backbone including AI and Data Science Tools
- **Finally, third year** was mainly focused on to the development of predictive modeling: Sequences, Expression patterns and regulation, Pathways, Protein- Function, Cellular phenotypes.

Among our technologies, we have developed several machine learning methods for phenotype prediction (subject to 2 patent applications). As example, we published a method to train a machine learning model to predict the phenotype of a biological object identified by its molecular

sequence. This in silico method has been validated by experimental in vitro data with WhiteLab's partner Genethon (see poster attached). Our algorithms are evaluated with gold standard metrics (accuracy, sensitivity, specificity) in the field of AI.

WhiteLab Genomics has developed a comprehensive portfolio of capabilities and products.

WLG is commercializing four products covering our main application and leveraging the full potential of our technological backbone:

- WE-KNOW: AI Powered Genomic Medicine Knowledge Machine
- WE-LOAD: Promoter Selection and Expression Cassette Design
- WE-MAP: Target Discovery and Cellular Biomarkers ID
- WE-VECTORIZE: Viral and Non-Viral, Capsid Engineering, Bioproduction optimization

Engineered and optimized therapeutic candidates are delivered to our partners and/or out licensed to biopharmaceutical companies for additional validation and development including in vitro and vivo studies.

Thus, we are fostering and de-risking the selection of the genomics materials candidates of tomorrow's therapies (and therefor our partners portfolio) with an improved success rate by predicting the best molecular design for genomic therapies based on predefined objectives. Over the past 4 years, WLG has successfully delivered more than 40 projects to academic, biotech and pharmaceutical companies across Europe and USA. As example,

- In February and May 2021, WhiteLab signs collaboration agreements respectively with Genethon and ART-TG, an INSERM laboratory expert in the pre-clinical development of gene therapies (see references),
- In December 2022, WhiteLab signs its first partnership with a leading pharmaceutical company,
- Early 2023, initiated a collaboration with SIREN, a new immuno-oncology start-up led by Nicole Paulk (former assistant professor at UCSF).

INNOVATION

There is significant untapped opportunity in the industry to scale AI within the GM value chain. Biotechnology companies enabled by machine learning (ML) that focus on novel modalities are still rare. Moderna is perhaps the most mature with a strong vision to have digital and analytics to boost its mRNA platform. In the past years, additional earlier-stage companies—including Modulus Therapeutics and Outpace Bio in the cell therapy space; Dyno Therapeutics and Patch Biosciences in the gene therapy and adeno-associated virus (AAV) space have emerged.

WhiteLab Genomics unique value proposition

At WLG, we empower our partners and customers to unlock the full potential of GM, by providing faster and cost-effective solutions for drug discovery, design, and development. Our distinctive approach centers around leveraging cutting-edge in-silico methods to facilitate the discovery, design, and biomanufacturing of genomic biotherapies. Also, our in-silico model ensures agility, enabling rapid adaptation and optimization throughout the research, development, and biomanufacturing phases. By embracing a hybrid partnership approach, combining collaborative R&D partnerships and service contracts. With this approach, we are generating strategic intellectual property assets and we are securing both short- and long-term revenues.

To accomplish this, we have developed a proprietary platform including algorithms and databases to improve the design of therapeutic vectors for enhanced safety and efficacy. These vectors can be viral, such as adeno-associated virus (AAV) and lentivirus, or non-viral, like lipid nanoparticles (LNPs). WLG synergistically combines computer science techniques, particularly Natural Language Processing (NLP), with bioinformatic methods like transcriptomic analysis and structure prediction. WLG employs data mining strategies and corresponding software modules to predict the most pertinent receptor-ligand interactions for specific targets, be it organs or cells. For instance, in the context of improved AAV transduction, WhiteLab strives to identify membrane-associated receptors and ligands that are highly relevant to a specific tissue. A key differentiator regarding our approach is that we can identify biomarkers that are highly specific to a cell type in over 850 organs in the body. This enables our AI platform to design the best vector to bring the right therapeutic sequence into the cells to be cured.

This approach holds tremendous potential for refining the efficacy and precision of vector delivery systems. Through our sophisticated software platform and integrative methodologies, WhiteLab endeavors to revolutionize gene and cell therapy R&D by leveraging vast amounts of knowledge and uncovering novel insights that facilitate the design of safer and more effective therapeutic vectors.

WLG is different from existing solutions or competitors' due to:

- A unique AI/ML platform specialized in the field of gene and cell therapy, addressing the full scope, from drug discovery, design, development to bioproduction.
- Public and non-public datasets thanks to proprietary Natural Language Processing, Machine Learning and Federated Learning algorithms
- A unique agile experience to customers thanks to our fully in-silico model

WLG enables companies to develop state-of-the-art gene and cell therapies faster, resulting in safer, effective treatment, greater patient access and reduced drug development costs.

REFERENCES

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