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Human Cell-Secreted Proteins Offer A Wellspring Of Potential Therapeutics

Interview With Rising Leader Hanadie Yousef

by David Wild

CEO Hanadie Yousef leads Juvena Therapeutics in utilizing an AI-based platform that analyzes cell-secreted proteins to identify potential therapeutics. One of their first near-clinical assets could complement GLP-1s.

Based in Redwood City, CA, *Juvena Therapeutics* employs advanced computing to map the 4,000 proteins secreted by human cells. Through an AI-enabled platform, the company can identify potential protein-disease relationships and engineer medicines accordingly. By integrating AI, robotics and other cutting-edge technologies, Juvena accelerates preclinical screening and advances promising candidates to in-house clinical development. The platform has already generated two assets ready for clinical trials and over 50 promising leads.

The company's lead asset is JUV-161, an engineered IGF-2 protein for subcutaneous injection for myotonic dystrophy Type 1, the most common adult form of muscular dystrophy. The biologic received a US FDA orphan drug designation in late 2023 and is set to start a Phase I trial this summer. Juvena will conduct additional trials in other myopathies and metabolic diseases, assuming it can raise sufficient funds. A series A round in late 2022 that was co-led by Mudabala Capital and Horizons Venture, with participation from several other funds, brought in $41m.

Further back in the development process, two other candidates targeting obesity present a significant market opportunity for Juvena, given the hot cardiometabolic market. One agent targets adiposity and the other targets muscle loss, which is an adverse effect of blockbuster

glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP) agonists.

Juvena's CEO and co-founder, Hanadie Yousef, a 2024 *In Vivo* Rising Leader, had a wide-ranging discussion with *In Vivo* about her career, the company's platform and the experience of starting a biotech.

Q When did you develop an interest in biopharma?

A My interest in science and biomedical research started when I was nine years old and decided to be a doctor. It accelerated when I began doing research at Regeneron Pharmaceuticals at the age of 15 and fell in love with the idea that we can leverage our discoveries and ideas to unlock new scientific discoveries and translate those discoveries into therapies that can help humanity. It was then I decided I wanted a PhD. I went to Carnegie Mellon University, majored in chemistry and continued doing research and through high school and college, I would go back to Regeneron for internships. That work landed me in a PhD program at UC Berkeley in chemical biology. At the time, I was really intrigued by gene therapy in oncology and wanted to dedicate my scientific career to developing and engineering viruses for site-specific integration to fix mutations.

During my first year of graduate school, I had a significant epiphany. I was interested in the notion that comprehending the mechanisms driving aging, particularly the alterations in protein signaling that contribute to bodily decline, including stem cell function, could be pivotal. By targeting these pathways and processes, we could potentially reverse the effects of aging, bolster tissue health, restore function, and achieve rejuvenation on various fronts.

Q **Why has the company decided to focus on the secretome as its scientific foundation?**

A The idea around Juvena stemmed from my PhD work at UC Berkeley, where my colleagues and I demonstrated that proteins secreted by stem cells, such as human embryonic stem cells, not only had the capacity to generate every tissue in the body, but had impressive regenerative effects across age-related disease in human cells and tissues and in aged animal models.

While people have known for decades about the therapeutic potential of secreted proteins –for example, insulin or human growth hormone – the therapeutic potential of these proteins remains untapped due to a combination of technical limitations and our inability to deconvolute these complex mixtures of thousands of proteins secreted by stem cells. What I noticed in looking at the biotech landscape was a

dearth of companies focused on unraveling the secretome to develop novel regenerative or tissue restoration-based therapies.

I didn't jump straight to starting a company. I continued with my dissertation thesis at UC Berkeley and did a five-year postdoctoral fellowship at Stanford, where I kept studying how protein signaling in our body impacts the health and function of core tissues, such as the brain and muscles. At the same time, I began networking and building the business model around Juvena because I knew that to really take that leap of faith and leave academia to go on an entrepreneurial journey and start the company, I needed a fellow co-founder and scientific expert that could complement my skill set. I had the great fortune to be in a serendipitous moment in 2017 and meet my co-founder, Jeremy O'Connell.

Q **Are there specific types of diseases that are most amenable to Juvena's approach?**

A Proteins secreted by human pluripotent stem cells can develop into any tissue and cell type in the body. Our platform maps proteins to specific cells and tissues, identifying their potential disease-modifying effects. We then translate and validate these findings in preclinical disease models. Subsequently, we develop methods to render them druggable, either by enhancing their drug-like properties through engineering or by modulating their pathways using alternative approaches.

We decided to first establish the framework of the platform focused on targeting metabolism and inflammation. The core tissues around metabolism and inflammation are muscle, bone, fat and, of course, the immune system. Our laser-like focus was on identifying proteins that can enhance muscle regeneration and improve muscle metabolism to treat diseases such as age-related muscle wasting and other diseases in which muscle wasting is core to pathophysiology. That led us to our lead protein therapeutic candidate, JUV-161, which we are developing for a rare orphan disease known as myotonic dystrophy type 1. Receiving FDA orphan drug designation last year was really validating.

In 2021, we started looking at adiposity and identifying proteins that can improve adipose metabolism and discovered our second nominated lead, JUV-112, which acts to enhance lipid metabolism to promote weight loss.

Q **What are the relative strengths of your pipeline obesity approach compared to blockbuster GLP-1s?**

A GLP-1s have been revolutionary and have opened so many doors in terms of how the pharmaceutical industry thinks about chronic indications, like the comorbidities that come with obesity, including cardiovascular disease, diabetes, fatty liver and other ailments that arise as we get older.

Juvena targets obesity from a different angle, which is identifying factors that can enhance lipid metabolism, which is what JUV-112 does. Unlike the GLP-1s, JUV-112 directly targets fat to promote weight loss and improve the health and composition of our body's organs. And we're doing it in a way where you don't have to starve yourself. Our mechanism does not induce appetite suppression. Based on what we have seen in our preclinical models and our data, this could be an opportunity to develop a complementary therapy for people who want to get treatment based on their comorbidities. It could also potentially be additive to the GLP-1s.

Q **Where do you see the company in 5-10 years?**

A In the near term, we are transitioning to the clinical stage. In the coming months we're going to be validating our approach to healthy aging in the clinic.

Our platform has generated over 50 hits to date, which is more than Juvena can develop alone, so I'm really hoping that in the near future we leverage the assets, the platform and the multiple early discovery programs to secure a couple of close pharma relationships. In collaboration we could potentially target some major chronic indications, which are, in my view, the largest unmet medical health needs of our time.