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Company Spotlight: Repair Biotechnologies

Reason CEO & Co-founder Repair Biotechnologies, Inc www.repairbiotechnologies.com

Repair Biotechnologies is pioneering the Cholesterol Degrading Platform. Can you explain how this technology works and the types of medical conditions it aims to address?

The Cholesterol Degrading Platform provides the ability to safely break down only excess free cholesterol inside cells via the delivery of optimized fusion proteins into a cell. All gene therapy approaches can work with our technology, but for our lead drug REP-0004 we have chosen to focus on lipid nanoparticle (LNP) delivery of messenger RNA (mRNA).

Excess cholesterol is a well-known contributor to various diseases. What are the limitations of current treatments, and how does your platform offer a safer and more effective solution?

Excess free cholesterol inside cells is toxic, a characteristic of aging, obesity, and a range of chronic and presently largely irreversible diseases in many different tissues. It contributes meaningfully to pathology in liver disease, atherosclerosis, and neurodegenerative conditions, but is an undruggable target. Cells do not naturally break down cholesterol, so no mechanism exists to manipulate with small molecules. Further, one cannot safely bind and sequester unwanted cholesterol to the degree needed without harming cells by also removing needed cholesterol. Further, targeting cholesterol transport has proven to have little effect on local deposits of excess cholesterol - e.g. one can't take statins to fix a fatty liver. Our drugs are the first to be able to selectively target and clear excess free cholesterol inside cells, and we have shown that this produces profound reversal of presently irreversible

What stage of development is the Cholesterol Degrading Platform currently in, and what milestones are you working toward in the near future?

We have just completed our first non-human primate study of REP-0004, demonstrating safety and the same metabolic changes as were observed in mouse models.



We obtained Orphan Drug Designation for treatment of the accelerated atherosclerosis of homozygous familial hypercholesterolemia, and have commenced the GMP manufacture process for REP-0004. We plan an IND submission and launch of a first clinical trial in early 2027.

How do you see Repair Biotechnologies contributing to the broader healthcare ecosystem, and what role does investment play in advancing your mission?

We hope to show that excess intracellular free cholesterol is an important target, and spur much greater attention to addressing it. There are too many conditions affected by this mechanism for one company to tackle alone; this will take an industry. Investment is vital for us to produce the clinical stage proof needed to convince the more conservative end of the pharma industry that we are right.

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Looking ahead, what excites you most about the future of cholesterol-related treatments and the role Repair Biotechnologies will play in shaping that future? What opportunities do you see for innovation and collaboration in the life sciences industry?

If looking back at what has been tried in terms of manipulating cholesterol metabolism, it is very onedimensional, very fixated on cholesterol transport. People have tried very little of what is possible in the grand scheme of things. Inducing a willingness to reexamine cholesterol from other angles is important: we have shown that sizable benefits in preclinical models of intractable diseases can result from this sort of research and development effort. Manipulation of cholesterol metabolism isn't boring and it isn't well-explored. Even just considering our specific approach of targeted clearance of only free cholesterol inside cells, there are scores of programs that might collaborate with us on treatment of a specific condition of aging or obesity. The field is wide open for novel directions.

