



UNCHAINING GENETIC MEDICINES: CHEAPER, SAFER AND LONGER- LASTING.

**Unlocking the Potential of Genetic
Medicines with Anti-Silencing DNA
Technology | Executive Summary**

HoudiniBio

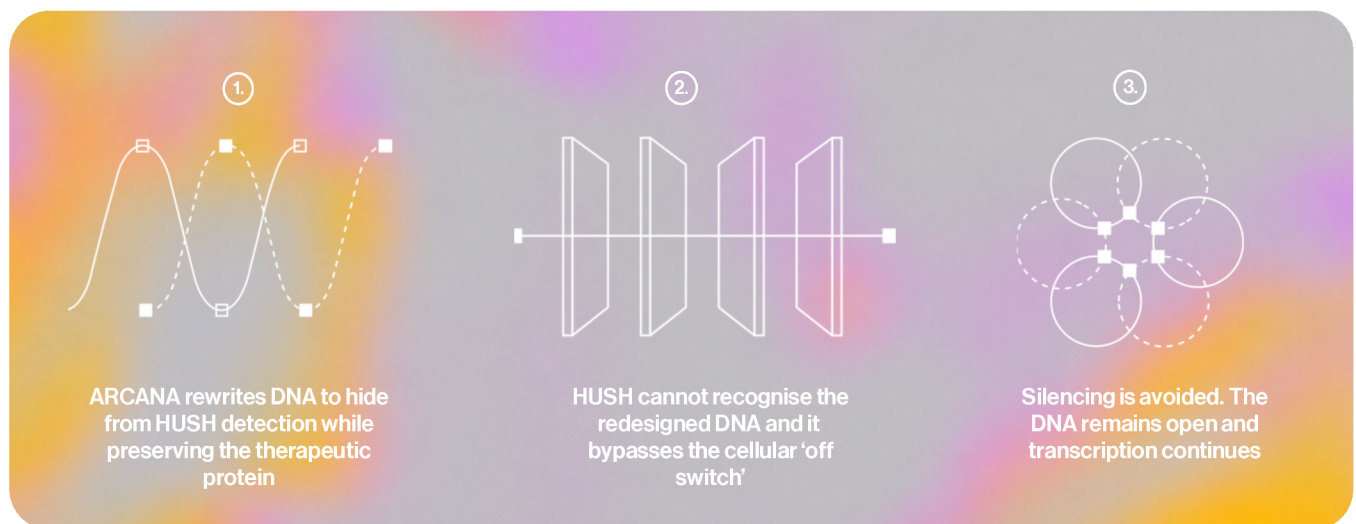
UNCHAINING GENETIC MEDICINES: CHEAPER, SAFER AND LONGER-LASTING.

Genetic medicines allow us to precisely target and treat disease. But therapeutic DNA is now bigger, more synthetic, and more complex. Unsurprisingly, it is recognised by cells as an intruder.

Cellular security systems which have evolved to distinguish self from non-self respond by silencing this DNA over time, capping potency, shortening durability, and preventing us from treating some diseases entirely.

This is an invisible ceiling- an unmapped limit which constrains patient outcomes and unit economics across the industry. We have created a brand new layer in therapeutic DNA design, built to lift that ceiling, addressing the root cause mechanism which enables expression of gene therapies at the highest efficiency.

Our AI platform, ARCANA, interprets and then engineers an escape route to the DNA silencing response, restoring sustained expression while preserving the intended protein product. The result is a universal, modality-agnostic boost to performance that compounds with everything gene therapy developers already use.



1000
trillion+

DNA copies required per patient to achieve a therapeutic effect

4-12X
improvement

in per dose expression versus state-of-the-art baselines

0-300
base pairs

the ultra compact size of our modifications

MARKET REALITY

Gene therapies are facing a multibillion dollar market adoption crisis. Their therapeutic efficacy can fade over time, leading to disease relapse in treated patients or preventing clinical endpoints from being met altogether. Production costs can routinely hit \$1M/dose, necessitating prices which the market is unwilling to pay, often accompanied by product discontinuation. High clinical doses also carry a major safety risk, leading to patient deaths and suspension of clinical programmes. Combined, this not only results in countless billions of dollars of unmet revenue for Pharma (across current and future pipelines), it also prevents patients from accessing life changing medicines.

Underpinning each of these challenges is the remarkable inefficiency of therapeutic DNA inside cells. Because of DNA silencing, a large fraction of DNA introduced into patients is eventually turned off. This explains poor therapeutic durability and disease relapse. It also explains the need for astronomical doses (1000 trillion+ DNA copies per patient), driving up production costs and toxicity.

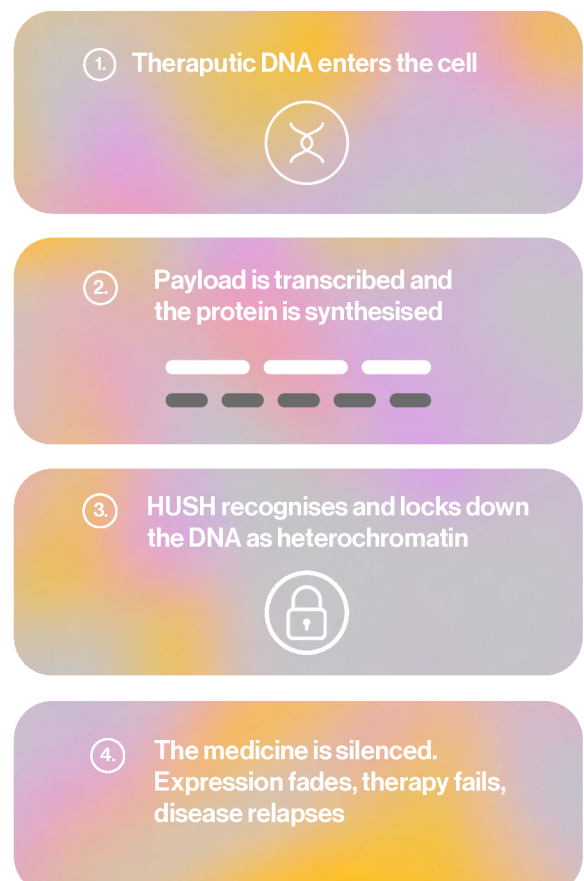
“This is an invisible ceiling-an unmapped limit which constrains patient outcomes and unit economics across the industry.”

DECODING OUR TECHNOLOGY | HUSH

The Human Silencing Hub (HUSH) is the cell's broad-spectrum defence against foreign DNA. First identified by our academic Co-Founder, Professor Paul Lehner at the University of Cambridge, HUSH recognises the very features which define therapeutic DNA payloads, including compact coding sequence, intron scarcity, and artificially engineered architecture. HUSH progressively converts foreign DNA into heterochromatin, transcription falls, potency per dose erodes, and long-term benefit fades.

As payload complexity rises, silencing pressure rises with it. That is why ostensibly curative gene therapies still lean on extreme, expensive dosing, why expression often wanes after an early peak, and why many drugs never make it past the clinical trial stage. Developers are colliding with a pervasive, unknown layer of regulation.

HUSH (The Human Silencing Hub)



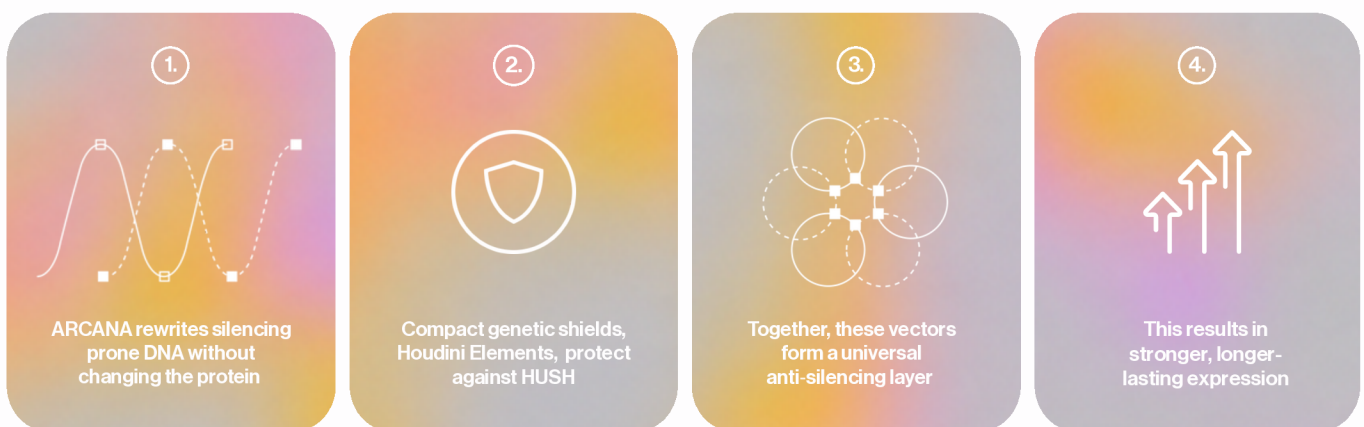
DECODING OUR TECHNOLOGY | OUR ENGINE

Houdini Bio's platform combines explainable computation with compact genetic components to neutralise silencing at its source in two ways:

Arcana is a predictive, in silico recoding engine. It analyses a transgene's architecture and silently rewrites the DNA to reduce silencing signatures without changing the amino acid sequence and without adding a single base pair. Arcana's zero-footprint uplift protects scarce vector space, accelerates validation, and improves potency per dose.

Houdini Elements are ultra-compact genetic shields, typically about 100-300 base pairs long, designed to buffer constructs against HUSH-driven repression. They are more than an order of magnitude smaller than many legacy stabilisers, making them compatible with tight packaging limits and complex designs. Elements stack with Arcana for compounded gains.

Together, these vectors form a universal anti-silencing layer which travels with the asset from discovery through manufacturing, improving performance wherever DNA expression matters.



"By compressing the cost stack, we lay the groundwork for global access that extends beyond the wealthiest health systems."

WHAT THIS UNLOCKS | COMMERCIAL

Gene therapy developers have proven it is possible to achieve life-changing outcomes. However, a huge fraction of these drugs won't reach clinical approval, trapping multibillion dollars in revenue and leaving patients unanswered. For therapies which reach the market, critical risks remain, including dose-linked toxicity, uncertain durability, and costs which strain payers and providers. Multiple FDA approved drugs have been withdrawn due to these challenges, turning peak sales forecasts from \$1Bn+ to zero.

Across a broad range of cell types, promoters, payloads and delivery vectors, Houdini Bio variants show between 4-12X improvement in per dose expression versus state of the art baselines, including an FDA approved AAV product. We've also shown large increases in durability of DNA expression over time versus state of the art comparators, improving the long term stability of therapy expression.

This level of uplift maps directly to dose-sparing strategies that reduce adverse events, enhance affordability, and make the one-and-done promise credible by supporting sustained therapeutic levels over time. For partners, this improves the probability of hitting pivotal endpoints tied to durable performance, strengthening the ability to achieve long-term outcomes-based reimbursement.

WHAT THIS UNLOCKS | HUMAN, ECONOMIC, AND SYSTEMIC IMPACT

Houdini Bio is built to improve rather than to replace. We work alongside therapy developers to make complex pipelines viable across indications. We prioritise:

- Preventing disease relapse and progression through durable gene therapy expression
- Making unit economics work through dose reductions
- Ensuring medicines are safe for all patients

For investors and commercial leaders, the value proposition is explicit: multibillion dollar asset unlocks, across current and future pipelines. For policymakers and payers, lower production costs and more efficient genetic medicines shift the conversation from rationing million-dollar therapies to broadening access. By compressing the cost stack, we lay the groundwork for global access that extends beyond the wealthiest health systems.

**INVISIBLE ENGINEERING.
VISIBLE IMPACT.**

**Learn more at www.houdinibio.com or
connect with us at lee@houdinibio.com**





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