



PRESS RELEASE | 17 MAY 2023

## Siren Biotechnology Launches to Pioneer Universal AAV Immuno-Gene Therapy for Cancer

- Novel approach combines the promise of two transformative therapeutic technologies, AAV gene therapy and cytokine immunotherapy, into a single transformative modality
- Believed to be the first ever AAV gene therapy for cancer and the first AAV gene therapy that can be made once and used for numerous indications
- Designed specifically to overcome delivery, efficacy and toxicity challenges associated with cytokine immunotherapies
- Siren to present first preclinical data today for new modality at ASGCT Annual Meeting
- Spin-out of the Paulk Lab at UCSF
- Founder and CEO Nicole Paulk, PhD, is world renowned expert in AAV gene therapy
- Initial funding led by Founders Fund and Lux Capital with participation from Innovation Endeavors, TechBio-focused ARTIS Ventures, Civilization Ventures and Savantus Ventures.

SAN FRANCISCO, CA [May 17, 2023] – Siren Biotechnology, pioneers of Universal AAV Immuno-Gene Therapy, a revolutionary new treatment modality for cancer, launched out of stealth today concurrent with its first preclinical data presentation at the ASGCT 26<sup>th</sup> Annual Meeting, taking place in Los Angeles, May 16-20th. Siren’s Universal AAV Immuno-Gene Therapy combines the promise of two transformative therapeutic technologies, AAV gene therapy and cytokine immunotherapy, into a single modality that is poised to redefine how tumor cells are destroyed and anti-tumor immunity is elicited. The company’s name was inspired by the powerful signal Universal AAV Immuno-Gene Therapy sends to the immune system, stimulating an immediate and comprehensive anti-tumor response. [Link here](#) for press release about Siren’s ASGCT presentation and preclinical data.

“The world needs big, bold, new ideas to fight cancer, and Universal AAV Immuno-Gene Therapy is exactly that. Our design and engineering of this modality redefines both AAV gene therapy and cytokine immunotherapy, and in doing so, changes the game for cancer treatment,” said Nicole Paulk, PhD, Founder and Chief Executive Officer of Siren. “This is the first AAV gene therapy for cancer and the first AAV gene therapy that is universal, meaning we can make it once and use it for numerous indications. This represents a huge leap forward for the AAV gene therapy field. We’re thrilled to officially launch Siren today and kick off that introduction with exciting preclinical, proof-of-platform data.”

“Unlike most ‘novel’ therapeutics in the biotech industry, Siren’s Universal AAV Immuno-Gene Therapy lives up to the adjective. Not only is there breakthrough therapeutic potential but Siren’s universal design can shorten clinical development and manufacturing timelines, and finally unlocks the possibility of helping patient populations on a larger scale than ever before in AAV gene therapy,” said Scott Nolan, Partner at Founders Fund.

Siren is a spin-out of the Paulk Lab at the University of California, San Francisco (UCSF), with initial funding led by Founders Fund and Lux Capital with participation from Innovation Endeavors, TechBio-focused ARTIS Ventures, Civilization Ventures, Savantus Ventures and others. A world-renowned expert in AAV gene therapy, Dr. Paulk sits on the Scientific Advisory Boards of and consults for multiple public and privately held AAV gene therapy companies. Since leaving her faculty role at UCSF to found Siren, Dr. Paulk has assembled a team of world-class scientific and industry advisors with deep leadership and expertise in clinical oncology, immunobiology, AAV engineering, viral production and manufacturing, and regulatory affairs, to work alongside the growing Siren internal team.

Siren’s Scientific Advisory Board and industry advisors include **Beverly Davidson, PhD**, AAV engineering expert, Children’s Hospital of Philadelphia, and Co-Founder of Spark Therapeutics; **Kaye Spratt, PhD**, AAV regulatory expert, and former Chief Regulatory Officer for BridgeBio Gene Therapy; **Susan Kaech, PhD**, brain tumor immunobiology expert, Salk Institute; **Carolina Lopéz, PhD**, fragmented viral genome immunogenicity expert, Washington University in St. Louis; as well as **Sharon Tetlow, MBA**, financial expert who has deep experience with biotech IPOs. Full bios for the Siren team and advisors are available at [sirenbiotechnology.com](http://sirenbiotechnology.com).

Dr. Paulk described how Universal AAV Immuno-Gene Therapy overcomes key challenges that have prevented cytokine immunotherapy from realizing its cancer-fighting potential to date: “Cytokine immunotherapy has been limited by several challenges, including cytokines’ profoundly short half-lives, toxicity associated with high-dose systemic administration, and off-target effects of non-specific cytokines. Merging the exquisite functionality of AAV gene therapy with the power of immunotherapy opens up a whole new world of possibilities to fight cancer. We enable long-term, steady, and controllable cytokine expression. We use self-limiting AAV genomes to deliver cytokines directly and only to the tumor. We ensure cytokine production directly in the local tumor microenvironment. It’s an elegant, multidimensional scientific and therapeutic solution.”

Brain and eye tumors are Siren’s first therapeutic areas of focus on its journey to re-invent solid tumor cancer therapy.

“We’re extremely impressed with the preclinical data in high-grade glioma that Siren is presenting publicly at ASGCT and are thrilled to be backing them. Brain and eye cancers, Siren’s initial focus areas, are devastating diseases with limited treatment options and have proven challenging to drug safely and effectively,” said Shaq Vayda, Principal at Lux Capital. “Siren’s approach is ideally suited to address the numerous hurdles that have plagued therapeutic

efforts against these notoriously difficult-to-treat cancers. Siren's off-the-shelf platform and universal design will enable them to rapidly build a pipeline of drugs for multiple brain and eye cancer indications and, ultimately, expand to other solid tumor cancers."

### **About Siren's Universal AAV Immuno-Gene Therapy's MOA and Safety Strategies**

Siren's novel modality is designed to deliver a swift, precise, and comprehensive attack on cancer by:

- 1) **Delivering vectorized, engineered cytokines directly to the tumor.** Siren's local gene therapy is precisely infused into the tumor, avoiding healthy cells.
- 2) **Rapidly killing tumor cells via endogenous targeted cytokine expression.** Siren's therapy destroys tumor cells in both resected and unresected tumors, including lingering tumor cells that are the primary culprit for recurrence in many cancers.
- 3) **Supercharging the innate immune response via cytokine expression.** Release of inflammatory cytokines from the infusion site activates the innate immune response by activating local macrophages and recruiting natural killer cells.
- 4) **Activating the adaptive immune response via antigen release.** Release of tumor and AAV capsid antigens from the dying tumor can activate an adaptive immune response by recruiting cytotoxic T lymphocytes.

Universal AAV Immuno-Gene Therapy is engineered with multiple layers of control to ensure unparalleled safety and differentiate this approach from other cytokine immunotherapy and AAV gene therapy approaches. These include self-limiting payload activity, an immunologically optimized AAV genome to limit non-specific immune system activation, and built-for-purpose vector integrity optimization.

### **About Siren Biotechnology**

Headquartered in San Francisco, CA, Siren Biotechnology is sounding the alarm against cancer. We are the pioneers of Universal AAV Immuno-Gene Therapy, which combines the promise of two transformative therapeutic technologies, AAV gene therapy and cytokine immunotherapy, into a single modality which we believe will redefine how we destroy tumor cells and elicit anti-tumor immunity. Our vision is for Universal AAV Immuno-Gene Therapy to become the standard of care for any solid tumor cancer.

To learn more, visit [sirenbiotechnology.com](http://sirenbiotechnology.com), and follow us on [LinkedIn](#) and [Twitter](#).

Universal AAV Immuno-Gene Therapy for Cancer. It's Here.

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