IAS 2021

CRISPR/Cas9 Gene Editing: From *Ex Vivo* to *In Vivo*

What is coming next for *in vivo* gene therapy?

Christopher Finch

CRISPR Therapeutics

Conflict of Interest Disclosure

- Full-time employee and shareholder of CRISPR Therapeutics

Summary for Community

- CRISPR gene editing holds promise for the treatment of a variety of serious diseases
- At CRISPR Therapeutics, we have demonstrated the potential promise of CRISPR gene editing in sickle cell disease and beta thalassemia
- We can apply the learnings from this work to other areas, including HIV
- Preclinical proof-of-concept studies suggest that CRISPR gene editing could provide complete protection against HIV
- Advancing from *ex vivo* editing of blood stem cells to *in vivo* editing could enable CRISPR/Cas9-based therapies for HIV that can benefit patients worldwide

The CRISPR/Cas9 Revolution

A **SPECIFIC**, **EFFICIENT** and **VERSATILE** tool for editing genes

Disrupt

Delete

Correct or Insert

"If scientists can dream of a genetic manipulation,
CRISPR can now make it happen"

Science

CRISPR Therapeutics Highlights

Leading gene editing company focused on translating revolutionary CRISPR/Cas9 technology into transformative therapies

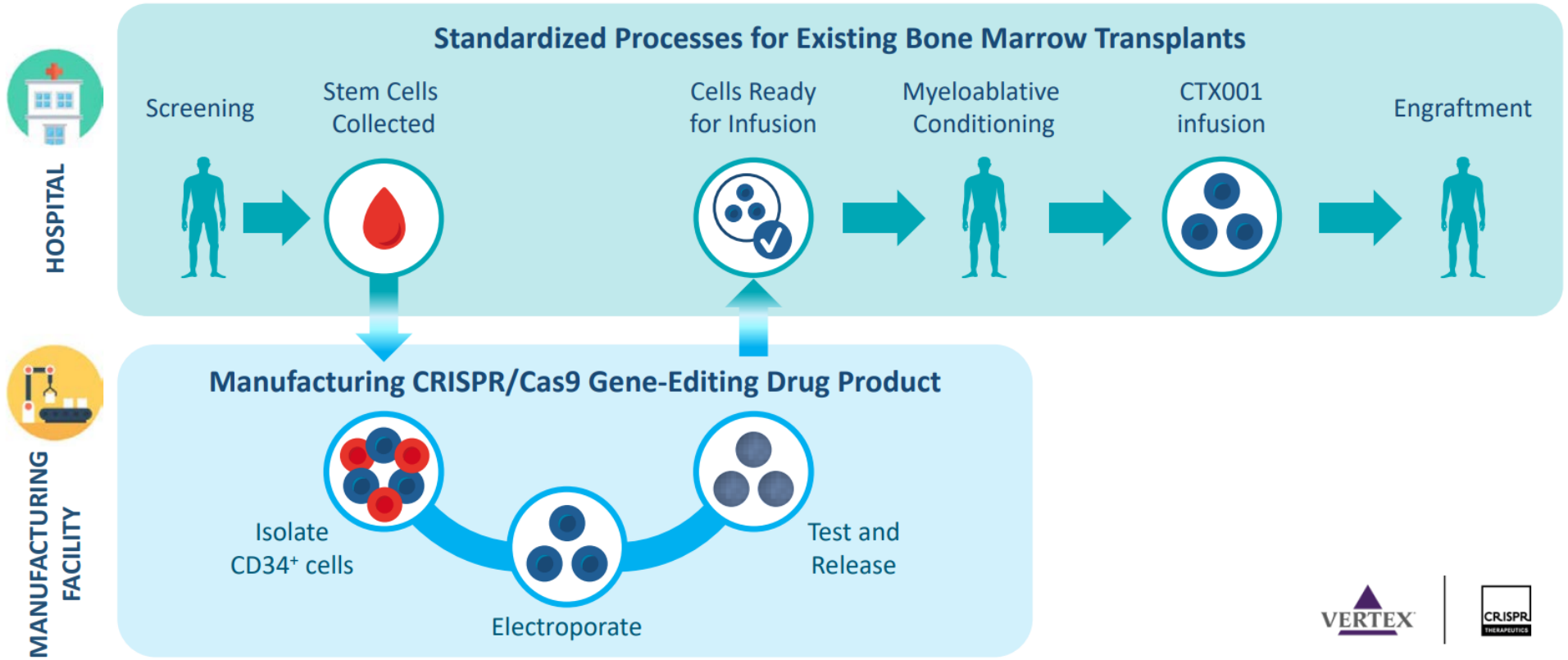
Advancing CRISPR in the clinic with CTX001™ in β-thalassemia and sickle cell disease

Next-generation immuno-oncology platform underlying wholly-owned, potentially best-in-class gene-edited allogeneic cell therapies CTX110™, CTX120™ and CTX130™

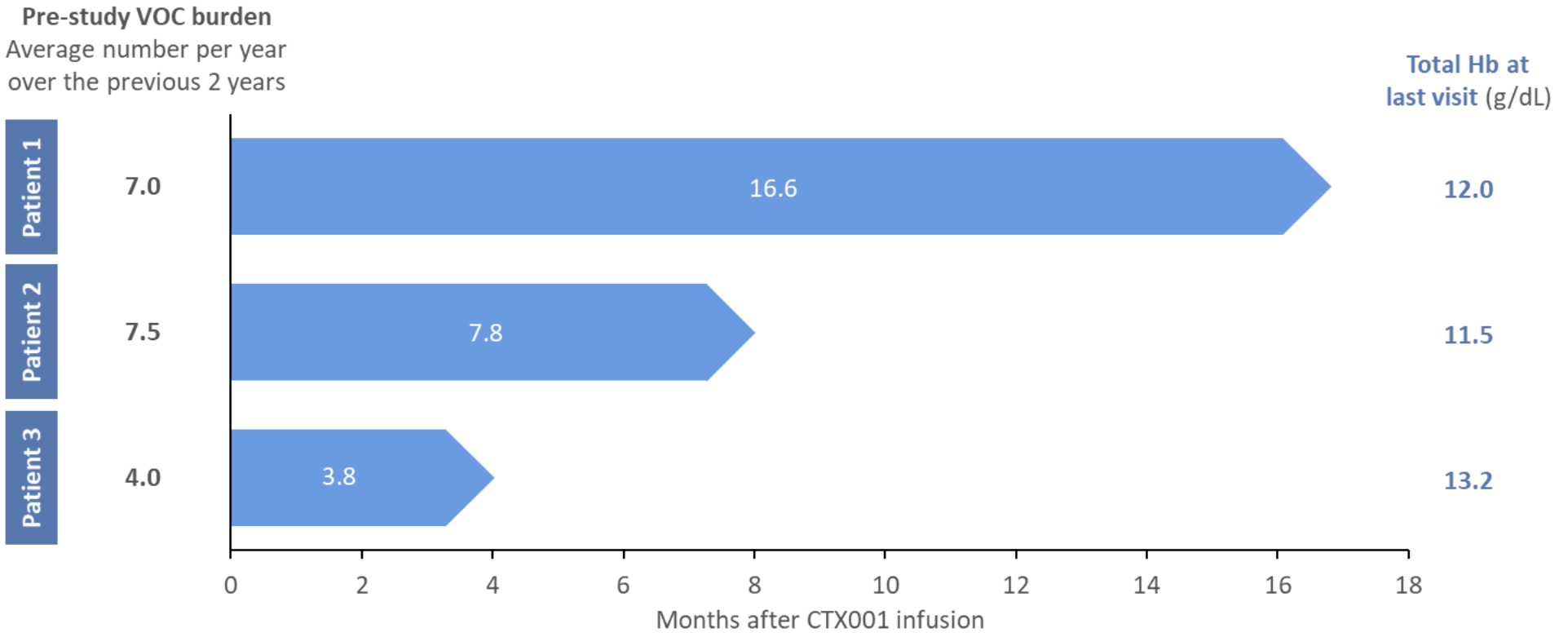
Enabling regenerative medicine 2.0 with CRISPR/Cas9-edited allogeneic stem cells

Advancing *in vivo* applications based on in-licensed technologies, platform improvement and strategic partnerships

CTX001™: *Ex Vivo* CRISPR/Cas9 Gene-Edited Therapy in SCD and TDT



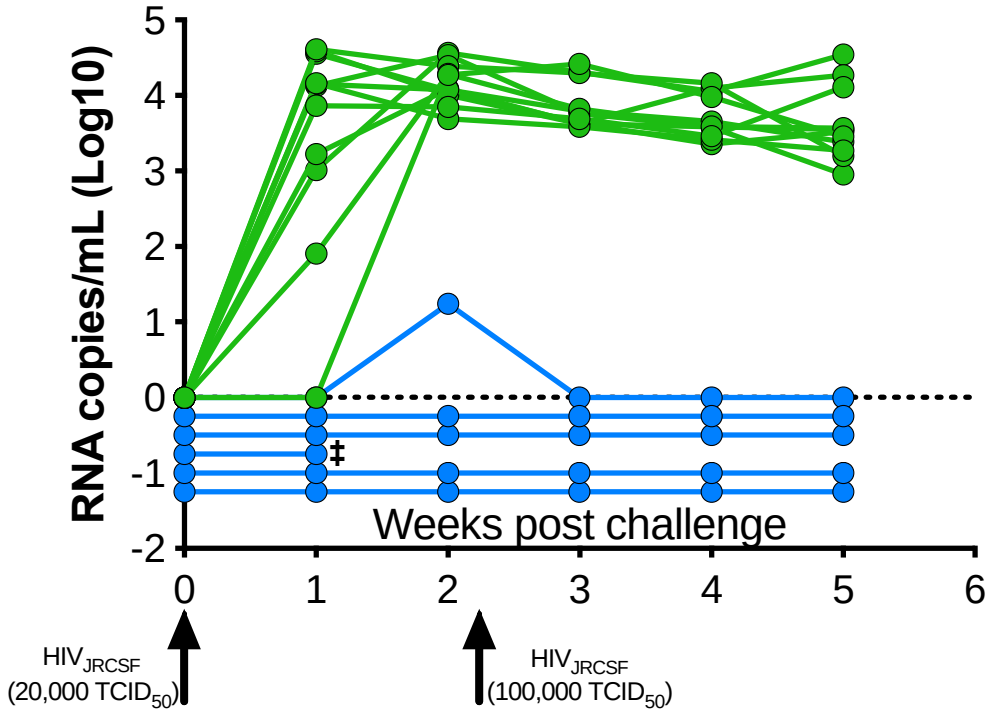
Duration Vaso-Occlusive Crisis-Free After CTX001 in SCD



All patients have detectable haptoglobin and improved LDH, indicating no evidence of hemolysis

Data disclosed December 5, 2020

Application in HIV: *Ex Vivo* Proof-of-Concept in Mice



All 8 control mice infected by CCR5-tropic HIV

All 5 CCR5-edited mice completely resistant to two HIV infection challenges at escalating doses

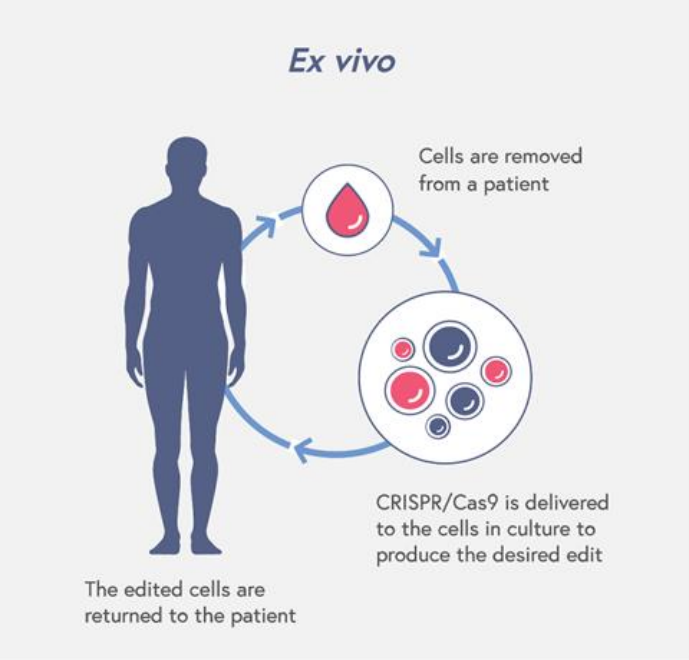
Mouse model:

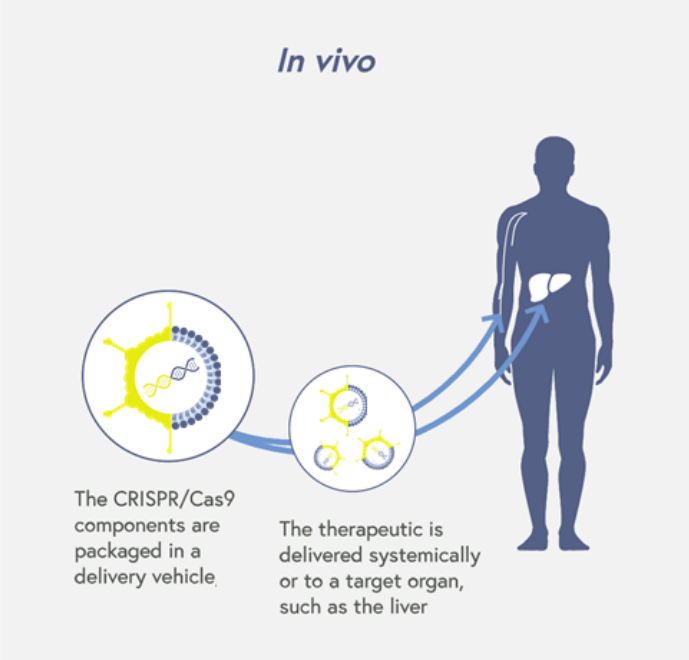
- Control (no editing)
- CCR5 edited

Research conducted in collaboration with

Ragon Institute of MGH, MIT and Harvard

From *Ex Vivo* to *In Vivo*





CRISPR Therapeutics Receives Grant to Advance In Vivo CRISPR/Cas9 Gene Editing Therapies for HIV

-Funding from the Bill & Melinda Gates Foundation will support research to enable CRISPR/Cas9-based therapies for HIV that can benefit patients worldwide-

Closing Thoughts

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