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# Actio seeks rare toeholds into common diseases with $55M A round

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Actio aims to leverage the target biology revealed by the strong genetic perturbations that drive rare diseases to treat a wider range of pathologies with shared phenotypic signatures.

"One of the strongest pieces of evidence we have for what these targets do are mutations that cause severe disease, for example, mutations that dramatically activate a channel," co-founder and CEO David Goldstein told BioCentury. "What are the phenotypic consequences of that activation?"

On Tuesday, Actio Biosciences Inc. announced a $55 million series A round led by Canaan and Droia Ventures, with participation from Deerfield Management and EcoR1, which participated in the company's $8 million seed round, and new investor Euclidean Capital.

Goldstein said the company, founded in 2021, is committed to its overarching strategy of addressing multiple indications via the same target, despite the potential for exposure to price-setting provisions established last year by the U.S. Inflation Reduction Act (IRA), which exempts orphan drugs that are approved for only one rare disease or condition, and no other diseases or conditions.

"Our thesis is there are rare diseases that can be highly informative about the role of a target in common indications. That is extremely valuable information to have, even in the face of any complexities the IRA creates," Goldstein said, noting the company could sidestep the challenge by developing different compounds. "You might learn in the rare disease with one compound, and then you might make a tailored compound appropriate for the common disease market."

As a researcher at Columbia University and Duke University, Goldstein and his lab pioneered methods to identify the mutations driving diseases likely to have genetic origins. These diagnostic genetic approaches, which involve filtering out common alleles, can now identify disease-causing mutations "reliably and at scale," but have had relatively little impact on patient care because of the dearth of treatments available for diagnosed rare disorders, he said.

Actio uses the company's human genetics platform, including its Rare Disease Target Atlas database, to identify genes with clear roles as disease drivers that preclinical models suggest offer opportunities to intervene after the onset of symptoms.

The company is focusing on small molecules, and developing its own compounds in-house. "We have prioritized targets where existing chemical matter gives us encouragement that we'll get a compound that acts the way we need to address these mutations," Goldstein said.

Other target prioritization criteria include data suggesting consistent biological effects across different disease-causing mutations in the same target, suggesting the same approach could apply to a range of rare disease patients.

The company's lead target, TRPV4, "had all these features," said Goldstein. "We are intending to treat all patients with rare diseases caused by mutations in TRPV4," including inherited neurological diseases like Charcot-Marie-Tooth disease 2C (CMT2C) and skeletal diseases such as metatropic dysplasia, he said.

Actio VP of Biology Sunil Sahdeo said the company has profiled over 60 disease-causing TRPV4 mutations in vitro, and conducted in vivo studies on recurring mutations using models developed by University of California Los Angeles and Johns Hopkins University researchers.

The company independently validates those results through its collaboration with The Jackson Laboratory, which will conduct "exhaustive" phenotyping of mutant mice that is "going to be a key part of generating pointers to common indications," Goldstein said.

Natural history studies and biomarker-rich clinical trials of Actio's candidates in rare indications will also build out the case for the targets' roles in common diseases.

"The plan is to use a more complete understanding of the disease phenotypes to think about ways to stratify common diseases based on signatures that relate to the target's involvement," potentially by identifying "a subset of a common disease that shows this signature," said Goldstein. Actio has not disclosed what common diseases it plans to pursue after its rare disease programs.

He said Actio's series A financing will enable the company to bring its lead program into clinic, and a second program to the candidate selection stage.

The most common molecular target for companies in BioCentury's BCIQ database with disclosed programs for Charcot-Marie-Tooth disease type 2 is the histone deacetylase HDAC6: Oryzon Genomics S.A., Augustine Therapeutics N.V. and Regenacy Pharmaceuticals Inc. each have preclinical programs against the target for CMT2, but none have disclosed they are specifically targeting the CMT2C subtype.

**COMPANY PROFILE**
**ACTIO BIOSCIENCES INC.**
San Diego, Calif.

**Technology:** Human genetics platform to identify rare disease targets with the potential to treat subsets of common diseases

**Origin of technology:** Internal

**Disease focus:** Neurology, musculoskeletal, dermatology

**Clinical status:** Preclinical

**Founded:** 2021 by David Goldstein and John McHutchison

**Academic collaborators:** University of California Los Angeles, Johns Hopkins University

**Corporate partners:** The Jackson Laboratory

**Number of employees:** 22

**Funds raised:** $63 million

**Investors:** Canaan, Droia Ventures, Deerfield Management, EcoR1, Euclidean Capital

**CEO:** David Goldstein

**Patents:** None issued

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