Fierce Biotech's 2021 Fierce 15

Tyra is striving to excel in three areas: crystallography, cell-based assays and in-vivo models

CEO: Todd Harris

Based: Carlsbad, California

Founded: 2018

Clinical focus: Overcoming acquired drug resistance

The scoop: The development of targeted cancer therapies follows a familiar pattern. A novel drug drives improved outcomes. Then, the cancer develops resistance, limiting the response rate and duration of efficacy. That pattern has played out across multiple targets such as FGFR, RET and ROS1. Tyra Biosciences wants to give patients with resistant tumors new, effective treatment options.

What makes Fierce: Resistance to targeted therapies is devastating to patients. Cancer has a way of resisting and recurring, and when it does patients are typically left without any good options. Tyra has made it its business to understand how cancers resist and recur, and develop drugs that get around those mechanisms.

That focus has led Tyra to excel in three areas: crystallography, cell-based assays and in-vivo models. Tyra identified the three areas as the key information its chemists need to help them design molecules that work in resistant tumors.

The problem is the information typically arrives at different times. Determining co-crystal structures of newly synthesized compounds can take weeks. In-vivo studies might be run every month or two. Tyra wanted everything to go faster to accelerate the iterative drug design cycle.

“We really made it our goal to figure out how we can get all that information done in a week so that when we hop on the phone with our chemists to design the next set of molecules, we know exactly where we need to take the chemistry,” Tyra CEO Todd Harris said.

Tyra has met its goals. The biotech has determined co-crystal structures in three days, generated results from cell-based assays in two days, and gathered data from in-vivo models in five days. Accelerating the crystallography process has enabled Tyra to refine structural designs using insights into changes that occur when a candidate binds to a target.

The platform has taken Tyra to the cusp of the clinic. Tyra’s lead candidate is a selective inhibitor of FGFR3, a fibroblast growth factor receptor that is also targeted by Johnson & Johnson’s Balversa and QED Therapeutics’ Truseltiq. Mutations can block access to a portion of the binding pocket accessed by first-generation drugs, leading Tyra to try to design a molecule that doesn’t interact with that site. By avoiding the back pocket, TYRA-300 retains its activity when a gatekeeper mutation emerges.

Tyra has also tried to improve on the safety and tolerability profile of existing drugs. After seeing that Balversa’s dose-limiting toxicity stems from interactions with FGFR1, Tyra worked to make its prospect more selective for FGFR3, a tough challenge given the similarity of the proteins. Tyra has preclinical data suggesting it rose to the challenge, with TYRA-300 proving to be far more selective than existing products.

The early successes have been achieved by a small team. Tyra had 16 full-time staff as of mid-August, almost all of whom worked in R&D. With clinical development on the horizon, Tyra filed to go public in August to support the expansion of its team and the progress of its pipeline.

Investors: Alta Partners, Boxer Capital, BVF Partners, Canaan, Cormorant Asset Management, Janus Henderson Investors, Logos, Nextech and RA Capital.

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