

13 May 2024 | Interviews

Ajax Set To ‘Attack JAK’ In Myelofibrosis With \$95m In Series C Cash

Will Advance Myeloproliferative Neoplasm Pipeline

by Mandy Jackson

Ajax Therapeutics plans to take its type II JAK2 inhibitor into the clinic during the second half of 2024 with the aim of modifying disease in a way that first-generation type I inhibitors do not.

[Ajax Therapeutics, Inc.](#) is going after an old target in myelofibrosis and other myeloproliferative neoplasms (MPNs) in a new way with its type II JAK2 inhibitor, AJ1-11095, which it will take into the clinic in the second half of 2024 now that it has closed a \$95m series C venture capital round. The company aims to generate deeper and more durable responses in myelofibrosis than seen with type I inhibitors, such as [Incyte Corporation](#)'s blockbuster Jakafi (ruxolitinib).

New York-based Ajax announced its series C financing on 13 May and said the US Food and Drug Administration cleared the investigational new drug (IND) application that will allow it to begin a Phase I clinical trial of AJ1-11095 in myelofibrosis patients whose disease has progressed after treatment with a type I JAK2 inhibitor, which may include Jakafi, [Bristol Myers Squibb Company](#)'s Inrebic (fedratinib), [GSK plc](#)'s Ojjaara (mometinib) or [Swedish Orphan Biovitrum AB](#)'s (Sobi's) Vonjo (pacritinib).

Key Takeaways

- Ajax raised \$95m in series C venture capital to take its lead drug candidate, a type II JAK2 inhibitor, into a Phase I clinical trial in myelofibrosis.
- The company and its name emerged from an academic consortium known as “Attack JAK,” which sought a better way of targeting JAK2 in the treatment of

Ajax emerged from an academic consortium of five doctors and researchers that called itself “Attack JAK,” which included experts in JAK biology and sought a new way of attacking the kinase, CEO Martin Vogelbaum explained in an interview with *Scrip*.

myeloproliferative neoplasms (MPNs).

- Ajax also will advance additional undisclosed R&D programs in MPNs.

“They had come together realizing that the current JAK inhibitors on the market for myelofibrosis and other myeloproliferative neoplasms were just coming up short to provide the level of efficacy and symptomatic relief for these patients and, most importantly, any form of disease modification to reverse the fibrosis, which is a hallmark of the disease, and probably most importantly to reduce the mutant clone that is responsible for the dysregulated erythropoiesis and platelet production,” Vogelbaum said.

The consortium had come to a point where it needed a company to step in and take the work it had done and the data it generated forward when an early benefactor of Attack JAK introduced consortium member and Ajax co-founder Ross Levine, a [Memorial Sloan Kettering Cancer Center](#) physician and [Weill Cornell Medical College](#) professor, to Vogelbaum.

Vogelbaum reached out to artificial intelligence-enabled drug discovery firm [Schrödinger, Inc.](#), also based in New York, to begin rapidly searching for a drug candidate targeting the type II conformation of JAK2. Ajax then launched with an initial \$8m in funding in 2019 and raised a \$40m series B round in June 2021. (Also see "[Finance Watch: Two New VC Funds Target Early Stage And Beyond](#)" - *Scrip*, 4 Jun, 2021.) Goldman Sachs Alternatives led the series C round with participation from [Eli Lilly and Company](#), Vivo Capital, RA Capital Management, Point72 and existing investors EcoR1 Capital, Boxer Capital, Schrödinger and Inning One Ventures.

Type II JAK2 Aims To Improve Efficacy, Durability

“This idea of going after the type II strategy came out of work that my and the David Weinstock ... labs had done in academia,” Levine told *Scrip*. Weinstock, an Attack JAK member, is now vice president of discovery oncology at [Merck & Co., Inc.](#), but previously was a physician and professor at the Dana-Farber Cancer Institute and Harvard Medical School.

“The current drugs – ruxolitinib, fedratinib, momelotinib and pacritinib – all bind the active conformation of JAK2, which is why they're called type I drugs,” Levine explained. “And we and David Weinstock had shown long before Ajax was created that the type I drugs have a liability in that JAK2 can still be activated by the other JAK kinases, even when it's frozen in the active state waiting to persist in signaling, and this both limits the extent of targeted inhibition and the durability of inhibition.”

The Levine and Weinstock labs showed that a type II inhibitor JAK2 inhibitor could deliver better efficacy than available type I drugs, but Ajax took that idea and make it into the drug – AJ1-11095 – that will move into the clinic later this year.

“What Ajax has is not only a unique binding, but we're binding the inactive conformation, so it doesn't have this accessory activation of the type I, so you get more potent activation and more durability, but it's also the most specific JAK2 inhibitor that's been developed so far,” Levine said. “And now we're going to find out if in the clinic that results not just in better improvement of the same things that current drugs do, like spleen size and symptoms, but do we begin to see, for example, changes in bone marrow fibrosis, the pathology and molecular responses.”

Vogelbaum noted that most myelofibrosis patients who start on JAK2 therapy, usually Jakafi, discontinue therapy at some point, primarily because they lose their response or don't respond to initial JAK2 therapy. And once they stop responding to a type I JAK2 inhibitor, they essentially run out of treatment options.

“The idea here is really to come up with an agent initially that can overcome this loss and lack of activity to the type I JAKs,” he said. “In preclinical models, consistently, we are able to re-sensitize the cells and the animals, at least, to respond and have actually better responses than the initial response that they had with the type I inhibitor.” Ajax hopes to show that AJ1-11095 can drive molecular remissions, impacting underlying causes of the disease, such as bone marrow fibrosis.

The expansion phase of Ajax's Phase I clinical trial will test AJ1-11095 in myelofibrosis patients whose disease has progressed after treatment with a type 1 JAK2 inhibitor. And if efficacy and tolerability are strong enough in the initial expansion phase of the trial in second-line treatment of myelofibrosis, an additional expansion phase cohort may enroll first-line patients, Vogelbaum said.

MPNs Remain Company's Main Focus

The company has not announced any drug candidates beyond AJ1-11095, but the rest of its research and development pipeline also is focused on treatments for MPNs.

“Our goal is to focus on areas where we think Ajax has unique core expertise and strength, and that both is within the JAK/STAT signaling pathway, and also in the myelofibrosis, myeloproliferative neoplasms and myeloid malignancies,” Vogelbaum said. “We have a number of projects ongoing in that space and we're going to continue to look at other opportunities, but we're always going to play to the areas which are in our wheelhouse.”

The company has six employees in New York and Cambridge, MA and contracts with outside firms, but does not have plans right now to grow its headcount significantly, the CEO said,

although Ajax may add people as its clinical-stage program gains momentum to keep the asset on track.