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Kinaset Advances Inhaled Pan-JAK Inhibitor For Broad Use In Severe Asthma

by Ayisha Sharma

Emerging Company Profile: The US biotech acquired its sole asset from CDMO Vectura in 2020 and is now gearing up for a Phase II proof-of-concept trial in severe asthma to help address the unmet need in non-eosinophilic patients.

Kinaset Therapeutics, Inc. is on a mission to create a convenient, inhaled treatment for severe asthma for use across the spectrum of disease phenotypes, including the insufficiently addressed non-eosinophilic subgroup.

The firm's roots can be traced back to the 2019 transition of former drug development firm *Vectura Group plc* into a CDMO. During the shift, Vectura chose to out-license its entire pipeline, including an inhaled pan-JAK inhibitor asset. A pulmonary physiologist by training, Kinaset CEO and co-founder Robert Clarke found himself drawn to this opportunity.

Key Takeaways:

- Kinaset's lead candidate, KN-002, is a pan-JAK inhibitor for severe asthma and COPD.
- KN-002 will enter three-armed Phase II proof-of-concept trial later this year.
- The inhaled drug could provide a more convenient option for some non-eosinophilic patients.

With the support of co-founders Roger Heerman and Frazer Morgan – now chief business officer and chief development officer, respectively – Clarke gained exclusive rights to the drug and

started looking for funding. In November 2020, the Medfield, MA-based company raised $40m in a series A with an eye to taking its candidate – dubbed KN-002 – through Phase II proof-of-concept for severe asthma.

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Asthma patients often begin treatment with inhaled steroids but, if these fail, they can move on to bronchodilators and eventually bronchodilators combined with steroids. Severe asthma remains uncontrolled despite these interventions, leading to exacerbations that can result in hospitalization. This is where KN-002 would fit into the treatment paradigm, the CEO told *Scrip*.

"You would add KN-002 to patients' existing treatment regimen to reduce the severity or incidence rate of exacerbations," Clarke said. Whereas most approved biologics for severe asthma – such as *Sanofi*'s Dupixent (dupilumab) and *AstraZeneca PLC*'s Fasenra (benralizumab) – target the IL-5 or IL4Rα receptors, KN-002 acts on all four JAK receptors (JAK1, JAK2, JAK3, TYK2).

"This pan action should give us the profile needed to treat both eosinophilic and non-eosinophilic asthma patients," Clarke explained, contrasting this with the current options, which are primarily effective for the former subgroup. Estimates suggest that 50% of severe asthma patients with non-eosinophilic disease do not benefit from treatment with approved IL-5 and IL4Rα monoclonal antibodies.

In 2021, the US Food and Drug Administration approved AstraZeneca and partner *Amgen, Inc.*'s anti-TSLP monoclonal antibody Tezspire (tezepelumab) for asthma without any phenotypic label restrictions. Although Tezspire is now an option for non-eosinophilic patients, it is administered via subcutaneous injection whereas KN-002 offers a more convenient mode of inhalation, Clarke highlighted. (Also see "*Keeping Track: Immunology Drives US FDA Action, With Approvals For AZ/Amgen's Tezspire, Argenx's Vyvgart, And New JAK Uses*" - Pink Sheet, 17 Dec, 2021.)

Since being founded in 2020, Kinaset has expanded its series A to $65m with the backing of an investor syndicate led by Atlas Venture and 5AM Ventures. Strategy-wise, the company is differentiated from other biotech firms in the respiratory space thanks to its "lean and mean" approach.

"Kinaset comprises just five people, but we all have twenty plus years' experience in developing respiratory therapeutics," the CEO said. "We're running a model that is completely outsourced – we use a CDMO for our formulation and CMC work."

The firm has also engaged a CRO for a planned Phase II trial in severe asthma to start in the

second half of the year. The three-armed study will set two undisclosed doses of KN-002 against placebo for 12 weeks in both eosinophilic and non-eosinophilic patients, measuring forced expiratory volume in 1 second (FEV1) as a primary endpoint.

Meantime, the drug candidate is currently under investigation in a Phase I/Ib dose-finding trial in patients with mild asthma, moderate-to-severe asthma and chronic obstructive pulmonary disease (COPD). The trial is now actively recruiting patients with COPD, which is another indication of focus.

Partnership Discussions Likely After Phase II

Regarding long-term development and commercialization, Clarke noted all options were on the table. “After reaching proof-of-concept, we think it would be advantageous to discuss with potential partners who have relatively greater resources when it comes to Phase III and commercialization,” he said.

“At the same time, we do have experience internally and me and another colleague have both been involved in running a publicly traded company in the past,” the CEO highlighted. If the Kinaset team were to go it alone, however, it would have to expand and grow accordingly, he concluded.