

## Interview - Astra deal breathes new life into Ethris's respiratory tech



[Jacob Plieth](#)

Delivery of mRNA into a cell has always been a tall order, and attempting this by the inhaled route must amplify the difficulty severalfold. But Ethris, a virtually unknown private German start-up, reckons it has cracked the problem.

"It may seem challenging, but we have worked on this for a couple of years," the group's chief scientific officer, Christian Plank, tells *EP Vantage*. The reward came yesterday, when Astrazeneca signed on the dotted line in a €25m (\$29m) deal that was about a year in the making, and whose focus on inhaled mRNA for respiratory uses will now shape development of Ethris's early portfolio.

Actually, Ethris had had an earlier partner, Shire, but that deal was canned after Shire's takeout of Baxalta a year ago. Rana Therapeutics, now known as Translate Bio, bought out some of Shire's mRNA work, but the Ethris asset, focusing on cystic fibrosis, was handed back.

At around the same time talks with Astra began, and it is noteworthy that the UK group was sufficiently persuaded in this time by Ethris's inhaled technology to strike yesterday's deal rather than expanding its more sizeable mRNA collaboration with Moderna ([Vantage Point - The messenger comes calling, July 23, 2015](#)).

### Therapeutic proteins

Unlike most of its peers Ethris is fully focused on delivering mRNA to generate therapeutic proteins - a far trickier application than using it to elicit an immune response and promote a vaccine effect.

Several mRNA players are in the clinic with vaccine approaches, but only Moderna has advanced a therapeutic candidate: mRNA AZD-8601, which encodes VEGF-A and targets undisclosed cardiovascular diseases, entered phase I in January. The big problem with therapeutic uses is how to avoid immunogenicity, the body's natural destruction of foreign RNA.

"Modified nucleosides are used to circumvent the activation of the innate immune system," says Mr Plank, adding that Ethris's IP centres on substituting a limited number of two nucleosides, uridine and cytidine. This, he reckons, is better than replacing all instances of just one nucleoside.

Then there is Ethris's internally developed delivery system, which is particularly useful for pulmonary delivery via inhalation. This makes use of certain polymers and lipidoids to encapsulate the mRNA and enable it to be aerosolised where in its naked form it would be destroyed.

"Your particles need to be stable enough to survive aerosolisation, you need to make sure they deposit in the right area of the lung, and they need to overcome the natural mucus barrier," says Mr Plank. And of course for every target one of the first studies is to prove that functional proteins are actually generated.

### Inhaled lead asset

Ethris's most advanced inhaled project, ETH-CFTR, is now its lead asset. This aims to generate the CFTR protein in cystic fibrosis patients, something also being attempted by Translate Bio, Arcturus, and most prominently by Moderna in a tie-up with Vertex.

However, CFTR lies outside Ethris's deal with Astra, whose focus is on asthma, COPD and idiopathic pulmonary fibrosis. Novel mRNA constructs will be used to make target proteins, with Astra having the [option to license these fully](#) and take them forward.

The deal is another sign that, despite making relatively quiet progress, developers of mRNA technologies continue to attract cash from investors and corporate partners. These include Curevac's \$110m private raise, Sanofi and Roche's deals with Biontech and of course Moderna's \$240m tie-up with Astra.

Ethris closed a series A round from HS Life Sciences and Orbimed, as well as attracting grant funding, but its head of corporate development, Gita Dittmar, will not disclose how much was raised. Astra's €25m is a "nice

addition to our coffers... and provides a significant runway”, she states.

Still, she denies that Ethris is in stealth mode, stressing that the company's focus must now be on execution. And even though there is a long way to go – an IND filing for ETH-CFTR is not expected until the second half of 2019 – she is determined to be patient: “I’d rather have something of value we’ve created to talk about than talk about something before we’ve done it.”

To contact the writer of this story email Jacob Plieth in London at [jacobp@epvantage.com](mailto:jacobp@epvantage.com) or follow [@JacobPlieth](https://twitter.com/JacobPlieth) on Twitter

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