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Novo makes a rare disease push

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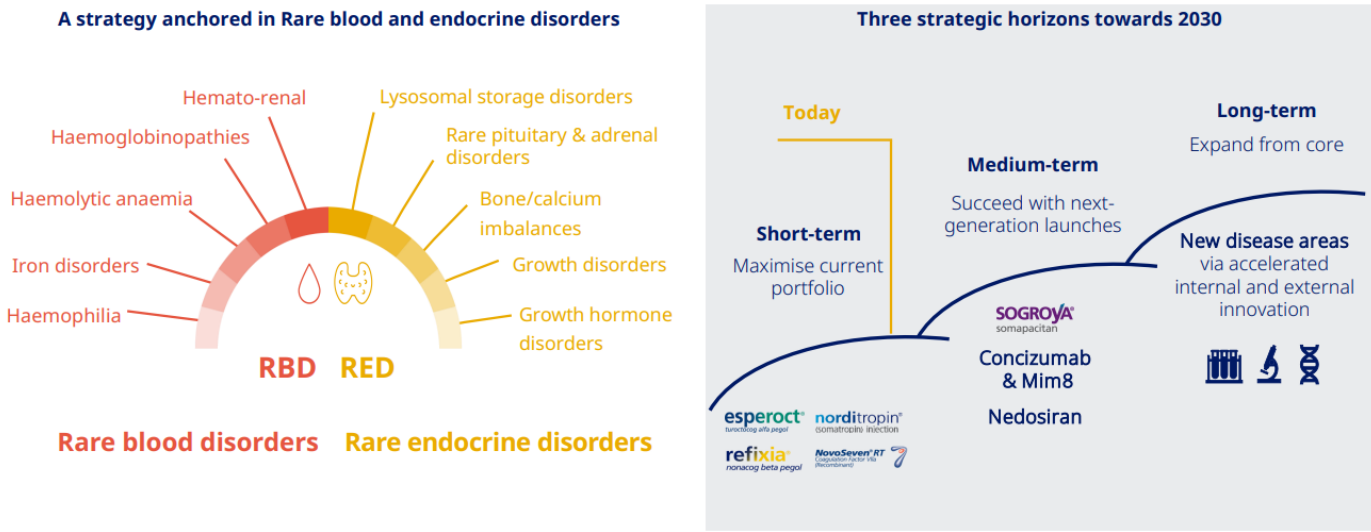
More deals could be in the offing, but gene therapy does not appear to be a big focus.

Novo Nordisk, which has historically preferred internal development to deals, has been more acquisitive of late. And the group's decision to double down on rare diseases, made official at its capital markets day last week, could lead to more purchases as it seeks to fill gaps in its portfolio.

A recent analysis by *Evaluate Vantage* found that rare diseases are a popular area for takeouts, so the Danish company will not be alone in its quest for targets. However, Novo's head of rare disease, Ludovic Helfgott, brushes off concerns about competition for assets. "What distinguishes us is that we're taking collaborations at an early stage. We are only interested in places where we can add value – we're not looking for super late-stage collaborations."

The group listed several areas of interest that fall under the broad umbrellas of either rare blood or endocrine disorders. Novo has chosen to stick with sectors in which it already has "legitimacy" via its existing haemophilia and growth hormone franchises, Mr Helfgott says.

Behind the renaming are ongoing efforts since 2019 to support the evolution and transformation of the Rare disease unit



Source: company presentation.

The pipelines of some of these therapy areas, such as lysosomal storage diseases, are crowded with gene therapy projects, but Mr Helfgott plays down Novo's interest in such technology. "We believe gene editing is more attractive for patients than gene therapy, because it's more durable."

To this end, Novo signed a deal in 2019 with Bluebird Bio over an in vivo gene editing asset in haemophilia A; this is now being developed in partnership with the Bluebird spinout 2seventy bio and is "progressing well", according to Mr Helfgott. However, 2seventy is otherwise focused on oncology, so it seems strange that this project did not stay with Bluebird.

Another "huge area of interest" for Novo is sickle cell disease, where it has an under-the-radar asset, known as Eclipse, about to go into phase 2. Mr Helfgott says the project, licensed from Epidestiny in 2018, it is an oral, fixed-dose formulation of decitabine and tetrahydrouridine, which is designed to deplete DNA methyltransferase 1 and thereby increase levels of foetal haemoglobin – various other sickle cell hopefuls are also working on boosting HbF (*A big year for sickle cell, February 28, 2022*).

He adds that Novo is investigating "several paths" in sickle cell, as he believes that "not one single drug will be the magic bullet".

Growth hormone deficiency

For now, though, the main focus for Novo's rare disease unit – formerly known as "biopharm" – is growth hormone deficiency and haemophilia. The Danish group sells several products here, including the daily growth hormone injection Norditropin and the recombinant FVII NovoSeven.

Several more could reach the market in the next couple of years. At the front of the pack is the once-weekly growth hormone Sogroya, which is already approved in adults and could soon have a shot at the more lucrative paediatrics market.

At the capital markets day last week Novo reported data from the phase 3 Real 4 trial in children, with Sogroya showing noninferiority to Norditropin on the primary endpoint, height velocity at one year. Regulatory filings are planned for the second quarter, but will noninferiority be enough, given that Ascendis's Skytrofa has shown superiority to daily injections?

"In growth hormone deficiency, regulators are extremely sensitive to the trade-off of efficacy versus safety," Mr Helfgott replies. "What we aimed at, from the beginning, was noninferiority to the daily drug. And that's what we got."

He adds that, if Sogroya does get the nod in children, other factors – such as the ease of use of the injector – could come into play; Novo's existing presence in the field might also help. Skytrofa's launch has disappointed so far, and Pfizer/Opko's rival weekly project somatrogon was recently knocked back by the FDA, so there is still all to play for here.

Haemophilia

In haemophilia Novo's next big hope is concizumab. The group reckons the project could be a universal

therapy, encompassing patients with the A and B form of the disease and those with and without inhibitors – echoing Sanofi's aim with fitusiran.

Last week Novo presented efficacy data from the phase 3 Explorer 7 trial in patients with inhibitors: the estimated mean annualised bleeding rate with concizumab prophylaxis was 1.7, versus 11.8 with on-demand therapy, and 64% of patients on concizumab had no bleeds. This puts concizumab about on par with fitusiran, according to data on the latter presented at last year's Ash meeting, with the usual caveats about cross-trial comparisons.

However, the problem with fitusiran is not efficacy, but toxicity: Sanofi's antithrombin inhibitor has been linked with blood clots and is now being tested at a lower dose.

Concizumab has a different mechanism of action, being a tissue factor pathway inhibitor, which should help it avoid this issue, Mr Helfgott says. Novo is not saying much about concizumab's safety profile in Explorer 7, but more details will emerge later this year. The project is also in Explorer 8, a phase 3 study in patients without inhibitors that completes in May.

Dicerna deal

Novo's late-stage rare disease pipeline is rounded out by the RNAi asset nedosiran, which the group gained through the recent $3.3bn purchase of Dicerna. Novo plans a regulatory filing by mid-year in primary hyperoxaluria 1 – nedosiran showed no effect in patients with the PH2 subtype – seemingly making the acquisition an exception to Novo's early-stage pledge.

But Mr Helfgott says: "The main purpose of the deal was not so much the asset; it was really the platform and knowledge." Novo has plans for RNAi, including delivering it outside the liver, and last week cited fat cells as an area of interest.

Mr Helfgott is adamant that Novo's renewed push into rare diseases is not down to pessimism around its core diabetes and obesity franchises. He believes that the group's primary care business can sit happily alongside an expanded rare disease offering. Now Novo just needs to prove that it can effectively target rare and common disorders alike.

This story has been updated to include more comments from Novo on the sickle cell project Eclipse.