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## Novo sets up antisense challenge with Staten deal



[Madeleine Armstrong](#)



### **Novo Nordisk's first cardiovascular collaboration could lead to an antibody versus antisense showdown in dyslipidaemia.**

Novo Nordisk said in September that it would expand into cardiovascular disease, and now it is putting its money where its mouth is. A partnership with Staten Biotechnology covering the latter's preclinical ApoC3 inhibitor could eventually see the Danish company going up against the likes of Ionis in patients with dyslipidaemia.

The Staten candidate, STT-5058, is an antibody, while other projects targeting ApoC3 take an antisense approach. Novo looks to be making a bet on a safer and cheaper alternative – although the group's head of drug discovery, Marcus Schindler, admitted that it will be a while before the project is put to the test in humans.

## ApoC3 projects in development

Company	Project	Pharma class	Indication(s)	Note
<b>Filed</b>				
Akcea (Ionis)	Waylivra	ApoC3 antisense	Familial chylomicronemia syndrome	CRL in Aug 2018
<b>Phase II</b>				
Akcea (Ionis)/Novartis	AKCEA-APOCIII-LRx	ApoC3 antisense	Hypertriglyceridaemia	Trial to complete Jan 2019 (NCT03385239)
<b>Preclinical</b>				
Staten Biotech/Novo Nordisk	STT-5058/ARGX-116	ApoC3 MAb	Hypertriglyceridaemia	
Arrowhead	ARO-APOC3	ApoC3 antisense	Hypertriglyceridaemia	
Wave Life Sciences/Pfizer	Apolipoprotein C-III Program	ApoC3 antisense	Liver disorders	
<i>Source: EvaluatePharma.</i>				

The most advanced ApoC3-targeting candidate is Waylivra, from the majority-owned Ionis business Akcea. Waylivra has been dogged by safety worries and got knocked back by the FDA in August; unmet need was not enough to outweigh concerns about the risk of serious bleeding and patient discontinuations ([Ionis feels the pain as the US FDA finally bares its teeth, 28 August 2018](#)).

Novo's Mr Schindler does not believe that these issues are down to the target, telling *Vantage*: "It could be a platform issue – the earlier-generation [antisense projects] obviously have some issues. We don't see a danger of running into similar adverse events with an antibody."

But the problems seen with Waylivra could be solved by next-generation antisense projects, he conceded. And Ionis already has such a candidate, AKCEA-APOCIII-LRx, which it is [investigating in a broader population of patients](#) with high triglycerides and cardiovascular disease.

A positive result could spur Novartis to license the project, potentially leaving Novo with a big rival to contend with.

### Cheaper and more convenient?

STT-5058 could still have several advantages over antisense projects, including price. However, this was "not a key consideration" for the deal, Mr Schindler said. "Yes, antibodies should have an attractive price play, but it's way too early to speculate on that, particularly as we don't yet know the dose or level of efficacy."

Novo plans to develop STT-5058 as a subcutaneous formulation, putting it in line with AKCEA-APOCIII-LRx. The Danish company is also working on oral delivery of large peptides and proteins which, if applied to STT-5058, could make it more convenient, but this technology is still very early stage.

When asked if there was a risk of lower efficacy with STT-5058, which is designed to clear ApoC3, versus antisense projects, which stop ApoC3 production altogether, Mr Schindler replied: "An antibody might have an advantage versus completely knocking out the gene – that's what we're going to figure out."

Further competition could come from Amarin's Vascepa, which recently scored a win in the Reduce-It cardiovascular outcomes trial. That product was designed to lower triglyceride levels, but its exact mechanism of action is not fully understood. Some, including Mr Schindler, believe that it could work at least in part via ApoC3. He added that, should omega-3 products become standard of care, Novo would hope to test STT-5058 on top of them.

It will be some time before it becomes apparent whether STT-5058, which originated at Argenx, will be a contender in dyslipidaemia: the project should go into humans in the next 18 months or so, Mr Schindler said.

Novo has an option to buy Staten if the data look promising. All the Danish company is saying about the deal right now is that it is worth up to €430m (\$488m), including milestones.

Mr Schindler is convinced that there is room for an ApoC3 antibody, even if antisense projects succeed and omega-3 therapy becomes entrenched. "There's still a huge unmet need. I think it's absolutely worthwhile to go after this modality."

*This story has been updated to clarify the delivery method for AKCEA-APOCIII-LRx.*

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[44-\(0\)20-7377-0800](#)

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