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Another complement factor enters the deal-making frame

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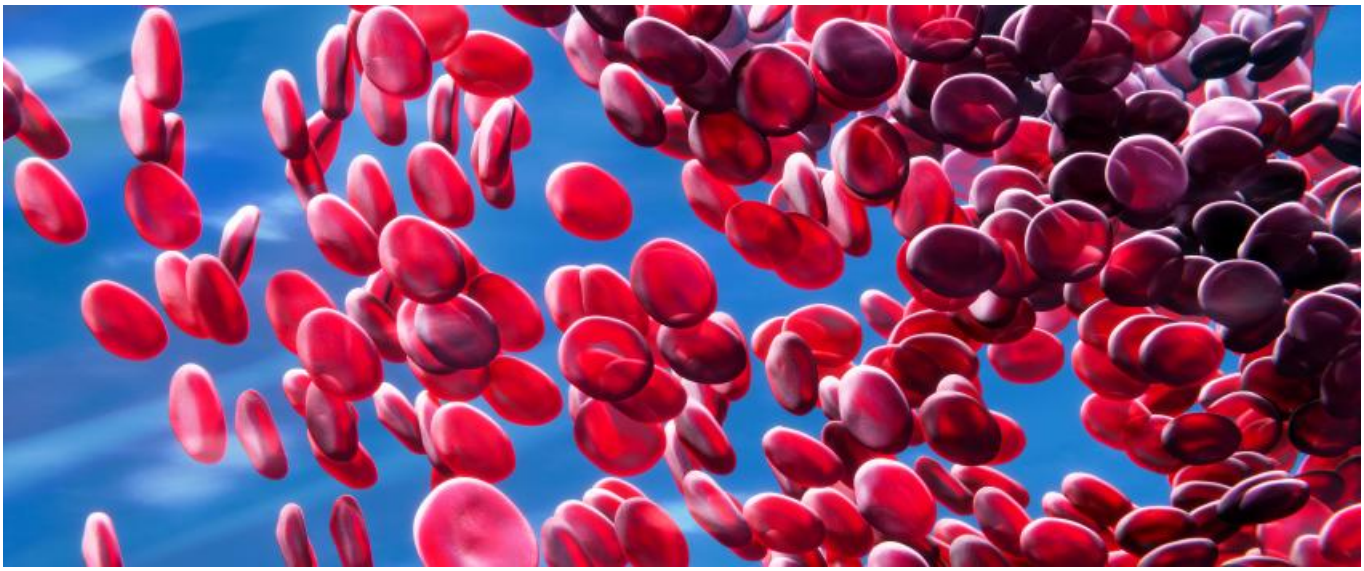

Sobi picking up rights to Apellis's complement factor C3 inhibitor adds to earlier deals focused on C5, D and anti-FcRn antibodies.

There has been much deal-making in treatments for complement-mediated diseases, so it was only a matter of time before Apellis's pegcetacoplan entered the frame. At $250m up front yesterday's tie-up with Sobi features at the low end of the valuation scale, but it does provide validation for a relatively novel mechanism.

Pegcetacoplan is a C3 inhibitor, a different approach from other complement factor-focused transactions, and one with relatively few competitors. For the time being, however, the focus will fall on the complex way rights to this molecule are being carved up, and how this could affect a takeover scenario.

The Sobi (Swedish Orphan Biovitrium) deal concerns ex-US rights to commercialise pegcetacoplan as well as global rights to co-develop it. It came nearly two years after Apellis first signed away rights to the molecule, in a transaction with the private US venture SFJ Pharmaceuticals worth $60m up front.

That earlier deal was described as novel and risk-sharing, but basically resembled a royalty monetisation set-up. The cash from SFJ was to be used for clinical development, initially for paroxysmal nocturnal haemoglobinuria (PNH), with SFJ getting its payback within six years of approval in the form of escalating milestones.

What the companies still lacked was marketing muscle; cue Sobi, which yesterday picked up rights to market systemically administered pegcetacoplan, with Apellis retaining US rights. Sobi stands to make milestone payments to Apellis, but presumably some of these will have to be paid away to SFJ.

Selected deals in complement-mediated diseases					
Project	**Originator**	**Company**	**Mechanism**	**Delivery**	**Status**
Zilucoplan	Ra	Company sold to UCB for $2.1bn	Complement factor C5 inhibitor	SC	Ph3 MG; ph2 PNH
Pegcetacoplan	Apellis	$60m milestone monetisation deal with SFJ Licensed to Sobi for $250m	Complement factor C3 inhibitor	SC	Ph3 PHN; ph2 CAD
ACH-4471	Achillion	Company sold to Alexion for $930m	Anti-complement factor D	Oral	Ph2 PNH
ALXN1830	Syntimmune	Company sold to Alexion for $400m	Anti-FcRn MAb	IV, SC planned	Ph2 MG
ABY-039	Affibody	Licensed by Alexion for $25m	Anti-FcRn bivalent Ab mimetic	SC	Discontinued
Source: EvaluatePharma. PNH=paroxysmal nocturnal hemoglobinuria; MG=myasthenia gravis; CAD=cold agglutinin disease.					

In a further twist, however, Apellis has carved out intravitreal pegcetacoplan (APL-2) a separate asset that it retains wholly.

Intravitreal APL-2 is expected to sell $1.4bn in 2026, according to *EvaluatePharma* sellside consensus, whereas the systemic carries a 2026 forecast of $641m. The former's lead indication is geographic atrophy, where the pivotal Derby and Oaks studies are due to read out late next year.

But it was haematology, specifically complement disorders like PNH and myasthenia gravis, that have provided the deal-making battleground. In November 2018 Alexion bought Achillion for $930m, and then a year ago it picked up Syntimmune for $400m while UCB spent $2.1bn on Ra.

Sobi, too, is apparently interested only in haematology, nephrology and neurology applications, which Apellis argues represent a population a third of the size of the one that intravitreal APL-2 might address. However, pegcetacoplan's big clinical win came in PNH (*Pegasus flies for Apellis, up to a point, January 8, 2020*).

Selected industry projects targeting complement factor C3		
Project	**Company**	**Possible indication summary**
Phase III		
Pegcetacoplan	Apellis/SFJ/Sobi	PNH, CAD, C3 glomerulopathy, ALS
APL-2 Intravitreal	Apellis Pharmaceuticals	Geographic atrophy
Phase II		
AMY-101	Amyndas Pharmaceuticals	C3 glomerulonephritis, PNH, periodontitis, Covid-19
Preclinical		
CB 2782	Biogen/Catalyst Biosciences	Geographic atrophy, dry AMD
Anti-C3 MAb	Otsuka (ex Visterra)	C3 glomerulonephritis
Source: EvaluatePharma.		

If complement inhibition is becoming crowded then at least Apellis can claim relative uniqueness. C3 inhibition, pegcetacoplan's mechanism, has relatively few competitors; C5 is the target for Soliris, Ultomiris and the Ra-derived zilucoplan, for instance, but C3 lies upstream of that, and Apellis claims that up to 70% of PNH patients experience low haemoglobin despite C5 inhibitor treatment.

However, it will not go unnoticed that the pegcetacoplan asset has now been split between two delivery formulations, and for one of these the rights are shared between three corporate entities. This type of setup could be hard to unwind, a burden on Apellis that might disappoint buyout bulls.

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