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Ash 2022 preview – Argenx’s expansion plans come into focus

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Vyvgart gets a prestigious press slot for its next potential use, while Sangamo’s haemophilia A gene therapy mimics Biomarin’s valrox again.

Argenx’s Vyvgart is expected to become a mega-blockbuster, but much still depends on the FcRN antagonist’s ability to expand beyond its current use, generalised myasthenia gravis. A study in immune thrombocytopenia (ITP) features in the press programme at this year’s Ash meeting, suggesting excitement around this approach.

Meanwhile, other non-oncology projects to watch at the conference include Roche’s crovalimab; Ash attendees are set to see the first phase 3 data on the anti-complement C5 antibody in the increasingly crowded indication of paroxysmal nocturnal haemoglobinuria (PNH). Still, these will come from a single-arm study in China, and more important readouts are approaching.

In the haemophilia A gene therapy space there will be a rare glimpse at Roche’s SPK-8011, acquired via Spark. And Sangamo’s Pfizer-partnered giroctocogene fitelparvovec continues to emulate Biomarin’s valrox by showing another fade in factor VIII levels at three years.

At least gir-fit appears to be back on track following the cases of very high FVIII levels that spurred a clinical hold of the pivotal Affine trial. The hold was lifted in September, and readout is due in the first half of 2024.

SPK-8011, meanwhile, does not appear to have started phase 3, although the project still featured in Roche’s most recent pipeline update.

Some are trying to get around the lack of durability problems that have been seen with factor VIII gene therapies. Poseida, better known for the Car-T portfolio that it recently licensed to Roche, will have preclinical data at Ash on its Takeda-partnered candidate, P-FVIII-101, which uses its non-viral Piggybac delivery system.

Selected Ash non-oncology abstracts				
Project	**Description**	**Company/ies**	**Abstract**	**Details**
Vyvgart (efgartigimod)	FcRN antagonist	Argenx	3	Advance in ITP; 22% response rate vs 5% with placebo
Crovalimab (RG6107)	Complement C5 inhibitor	Roche	293	Commodore-3 single-arm Chinese PNH trial; 79% haemolysis control
SPK-8011	FVIII gene therapy	Roche (Spark)	783	Up to 5-yr data from ph1/2 & LTE in haemophilia A
Giroctocogene fitelparvovec (SB-525)	FVIII gene therapy	Sangamo/Pfizer	3461	3-yr data from ph1/2 Alta in haemophilia A; FVIII levels continue to fade
P-FVIII-101	FVIII gene therapy (using PiggyBac delivery)	Poseida/Takeda	400	Preclinical data
OTL-201	SGSH gene therapy	Orchard	782	Ph1/2 in MPS-IIIA; 5 pts; first neurocognitive data due
RP-L301	PKLR gene	Rocket	2138	RP-L301-0119; 2 adults with PKD had normal-range Hb 18mth post-infusion
RP-L201	ITGB2 gene therapy	Rocket	3460	RP-L201-0318; 100% OS at 1 yr in 9 pts with LAD-I (previously disclosed)
RP-L102	FANCA gene therapy	Rocket	4775	Efficacy seen in 5 of 9 pts with Fanconi anaemia across trials

LAD-I=Leukocyte adhesion deficiency-I; MPS=mucopolysaccharidosis; PKD=pyruvate kinase deficiency. Source: Ash.

Poseida has a long way to go, unlike Argenx, which will hope to add another string to its bow soon. The Vyvgart data come from the Advance trial of the intravenous formulation of the drug; this was toplined as positive in May.

The company says there is no clear standard of care for ITP, which causes excessive bruising and bleeding; current options include steroids and the blood cancer drug Rituxan. Patients in Advance were heavily pretreated, with 67% receiving three or more prior therapies.

Of 118 chronic ITP patients, 22% of those receiving Vyvgart achieved a sustained platelet response, the primary endpoint, versus 5% of the placebo group, according to the abstract. Still, Vyvgart did not significantly decrease the incidence of WHO-classified bleeding events, a secondary outcome.

A study of the subcutaneous formulation of Vyvgart in ITP is set to report in the second half of next year. In the nearer term, the Adhere trial in another new indication, chronic inflammatory demyelinating polyneuropathy, could unlock a “multibillion-dollar market” according to SVB analysts.

PNH push

If ITP is an underserved disease, PNH is shaping up to be the opposite, with various players aiming to take a bite out of the current market leader, Astrazeneca.

Roche is one of these hopefuls. It has already filed crovalimab in China on the back of the uncontrolled Commodore-3 study, data from which will be presented at Ash.

However, the bigger test will come in the global Commodore-1 and 2 trials, which aim to show non-inferiority of subcutaneous crovalimab versus Astra’s intravenous Soliris. Whether this will be enough, with oral options like Novartis’s iptacopan coming, is a big question. Roche plans US and EU filings for crovalimab next year.

Elsewhere, the beleaguered gene therapy specialist Orchard is promising the first cognitive outcomes data on OTL-201, a gene therapy for Sanfilippo syndrome type A; biomarker data have previously been reported.

And Rocket will have data on its three lentiviral projects, including two that are set to be filed next year: RP-L102 in Fanconi anaemia and RP-L201 in leukocyte adhesion deficiency-I. In pyruvate kinase deficiency there will be adult data on RP-L301; investors will have to wait for next year to see if results can be replicated in children, and a pivotal trial is due to start next year.

The Ash conference is due to take on December 10-13 in New Orleans, Louisiana.