Evaluate Vantage

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Ash 2019 winners and losers

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Data and M&A lifts buoyant biopharma companies from Fate Therapeutics to Rocket, though on share price gain Forty Seven wins Ash 2019.

The American Society of Haematology conference is the final big medical meeting of the year, and data updates can help determine whether the biopharma sector ends the year with a bang or a whimper. The former looks most likely, as things currently stand: Ash saw notable progress reported in some closely-watched fields, from bispecifics to targeted oncology.

A handful of deals in related fields were also announced over the period of the conference, helping to maintain the biopharma rally that started in early October. Ash did contain some disappointments, of course, though the buoyant market conditions helped to contain losses, to the extent that few meeting-related stocks were sitting on serious declines as the conference came to a close.

The analysis below tracks share price performances from November 6, when Ash abstracts were first released, to the end of the conference on December 10. This extensive period means that the true Ash effect is hard to quantify for the larger players, though for several of the smaller drug developers the impact is clear.

Forty Seven, for example, was, until the Ash abstracts were released, struggling to convince investors that its anti-CD47 approach had legs – understandable given little progress elsewhere (*"Don't eat me" competition finds Celgene discontinuation hard to digest, October 10, 2018*).

However, data from an ongoing phase Ib trial of the company's lead project, magrolimab, showed startlingly good responses in patients with untreated myeloid malignancies. This included 22 patients with myelodysplastic syndrome, in which magrolimab plus azacitidine induced a 92% overall response rate, half of which was made up of complete responses.

In 22 acute myeloid leukaemia patients, an ORR of 64% was reported, of which 41% were CRs. Numbers remain small, however, and median duration of response has yet to be reached, an important future read out. Still, the data compare favourably to Abbvie's Venclexta here – this also reported data at Ash in a similar patient pool. An ORR of 77%, with a CR rate of 39%, was generated in 57 MDS patients.

Forty Seven made the most of its share price jump by raising almost $200m, which should see the company to the FDA. It hopes to file magrolimab for approval in 2021.

Notable Ash 2019 movers		
Company	**Share price chg Nov 6 - Dec 12**	**Notes**
Forty Seven	333%	Phase Ib data on magrolimab
Arqule	150%	Phase I data on ARQ 531, bought by Merck & Co for $2.7bn
Aptose Biosciences	65%	Two poster presentations, up on Arqule take out
Rocket Pharmaceuticals	63%	Phase I data on RP-L102, also up on Audentes takeout
Principia Biopharma	50%	Phase I/II update on PRN1008, up on Arqule, Sanofi news.
Fate Therapeutics	41%	FT516 data press released alongside incremental Ash updates
Agios Pharmaceuticals	31%	Updates on mitipivant in thalassemia and PK deficiency
Uniqure	28%	Update on haemophilia project AMT-601
Constellation	26%	CPI-0610 data in myelofibrosis
TG Therapeutics	23%	Poster on BTK inhibitor TG-1701, up on Arqule take out
Xencor	19%	Early data on XmAb13676, up on bispecific buzz
Precision Biosciences	18%	Up then down on PBCAR0191 update
Blueprint Medicines	-4%	Safety concerns crimp hopes for avapritinib
Sangamo Therapeutics	-4%	Brought down by ST-400 update?

The takeout of Arqule, for its BTK inhibitor ARQ 531, helped lift other companies working in this space. While the deal confirmed the potential seen in BTK inhibition, ARQ 531 data at Ash added flesh to the story. The non-covalent project showed impressive responses in patients who had become resistant to covalent BTK inhibitors – Johnson & Johnson's Imbruvica or Astrazeneca's Calquence – helping to explain Merck's interest.

Early data on a new version of Rocket's gene therapy for a rare form of anaemia, RP-L102, gave the company's shares a boost. Two treated patients are showing signs of engraftment, the company said, with no major safety issues seen. The takeover of gene therapy company Audentes by Astellas will also have given Rocket a lift, along with companies like Uniqure (*Astellas spends $3bn on a bold move into gene therapy, December 3, 2019*)

Principia shares hit a high in the wake of the conference, though the uplift was probably more to do with a halo effect around BTK inhibition – the company's own project, PRN1008, reported incrementally interesting data in immune thrombocytopenia at Ash. As well as the focus of the Arqule takeout, Sanofi highlighted an in-house BTK project as one of six high priority programmes, which added to the attention on Principia.

Fate Therapeutics provided updates on a couple of projects over the Ash weekend which, despite containing little clinical data, gave the stock a 41% uplift on the Monday. It was data not being presented at the conference that generated the most excitement. At an investor event the company detailed evidence that FT516, an off-the-shelf NK cell therapy that has only been given to two patients so far, is working in one patient with AML.

Progress with simpler cell therapy approaches was an overriding theme of Ash, in contrast to the complexities of autologous Car-T therapies that have made it to market. Progress in the bispecifics space, for example, lifted small companies like Xencor; the leaders here are Regeneron and Roche, which advanced 13% and 1% respectively over the period analysed.

Going down

Blueprint was a rare loser: a phase I study of its kinase inhibitor avapritinib generated encouraging responses in mastocytosis patients, but safety remains a sticking point. A fatal brain bleed in one patient took a lot of shine off the data.

Sangamo, too, fell over the period in question, despite an Ash presentation of an encouraging update with its haemophilia A gene therapy which is partnered with Pfizer. Five patients have been treated with SB-525, and have reported big increases in clotting factor that have been sustained as far out as 44 weeks.

A post-Ash plunge coincided with announcement of results from the first three patients to be treated with ST-400, an ex-vivo gene edited beta thalassemia project. This contained nothing dramatically worrying, and investors continue to scratch their heads over the plunge in Sangamo shares this week.

Finally to Precision Biosciences, which remains up over the period, despite crashing 52% on Monday. The stock had climbed into the conference on hopes for its CD19-targeted allogeneic Car-T project, PBCAR0191, which has been tested in nine patients to date. But the presentation contained disappointing response rates and some early relapses.

Below is a summary of more detailed *Vantage* coverage over the period, including analyses of the intensely competitive BCMA-targeting space and growing evidence of bispecifics' place in haematological cancers. Until next year...

Vantage's Ash 2019 coverage	
December 7	*Johnson & Johnson overshadows Bluebird's registrational reveal*
December 7	*Roche doesn't disappoint with bispecific*
December 8	*Former Celgene holders look anxiously at contingent value*
December 9	*For Car-T the bispecific antibody threat is real*
December 9	*Merck gets Arqule ahead of data*
December 10	*Regeneron takes the bispecific baton and runs*
December 10	*Quazar shines for Bristol*
December 10	*Sanofi gets a warm reception for Bioverativ asset*