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Upcoming events – Bluebird showcases its CAR-T approach while Medgenics aims for mGluR

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Next week Bluebird will report early data from its phase I trial of bb2121, an anti-BCMA CAR-T project, in multiple myeloma, prompting comparisons with competitor offerings as this year's Ash meeting gets under way.

Medgenics is expecting results from a phase II/III in ADHD trial by year end, testing NFC-1, a metabotropic glutamate receptor (mGluR) modulator, in patients with receptor mutations. Efficacy and safety setbacks have followed the mGluR class, and Medgenics will be hoping that its targeted approach does not follow suit.

Early bird

Bluebird's efforts in CAR-T therapy took a hit when its partner Celgene stepped back and struck a deal with Juno, and its focus here is now on the BCMA-targeting project bb2121.

The phase I multiple myeloma trial of bb2121 began in January, and Bluebird surprised the markets last week when it said the first clinical data from this would be revealed at the EORTC-NCI-AACR Molecular Targets and Cancer Therapies symposium on December 1. Since the start of November the group's stock has climbed 30%.

It is not clear how many of the 50 patients due to be enrolled have been dosed, or how many will be included in the data available at the meeting. The presentation will likely detail bb2121's safety profile and efficacy data – perhaps relating to responses with short follow-up – might also be outlined.

Investors will be comparing bb2121 against the NCI's slightly different anti-BCMA construct, which uses gamma-retroviral rather than lentiviral transfection. Both programmes are led by the NCI's Dr James Kochenderfer, who at an update in March reported that four of 12 patients given the NCI's version went into remission, though one relapsed after 17 weeks.

Bluebird will soon face additional competition, and recently Juno and Kite started working on CARs against BCMA, an antigen present on plasma cells. At next month's Ash meeting Novartis's partner the University of Pennsylvania is presenting clinical data on another anti-BCMA CAR-T project, while Cellectis and Pfizer have preclinical data on UCART-BCMA, an allogeneic approach.

Surprisingly, there is no Ash update on Dr Kochenderfer's BCMA work at the NCI. He had earlier hinted that most of his effort was going into the Bluebird study, and doubtless investors will see this as another positive for the company.

Subpopulation

Medgenics is conducting a phase II/III trial in 90 adolescent patients aged 12-17 with mGluR mutation-positive ADHD. The company says mutations affecting glutamate neurotransmission can be causally associated with ADHD, and are present in up to 25% of children with the disorder. A saliva-based diagnostic is used to determine genotype.

The double-blind, placebo-controlled study, Saga, should report by the end of the year. NFC-1, also called MDGN-001, is an mGluR activator, and the trial is testing oral doses of 100mg, 200mg or 400mg twice daily, measuring change from baseline in ADHD rating scale at six weeks as primary endpoint.

A phase Ib trial was run by Neurofix Therapeutics, a spin off from the Children's Hospital of Philadelphia that Medgenics acquired last year, in 30 adolescent ADHD patients with disruptive copy number variants (repeated regions of DNA) in glutamatergic genes. In this open-label five-week trial NFC-1 was generally safe and well tolerated, and patients showed clinical improvements in symptoms in response to escalating doses.

Targeting the metabotropic glutamate receptor					
Status	**Project**	**Generic name**	**Mechanism**	**Company**	**Indication**
Phase II/III	NFC-1	fasoracetam	mGluR modulator	Medgenics	Attention deficit disorder/hyperactivity
Phase II	Dipraglurant-IR	dipraglurant	mGluR5 antagonist	Addex Therapeutics	Parkinson's disease
Phase I	Pomaglumetad Methionil	pomaglumetad methionil	mGluR2/3 agonist	Lilly/Denovo Biopharma	Schizophrenia
	Dipraglurant-ER	dipraglurant	mGluR5 antagonist	Addex Therapeutics	Focal cervical dystonia
	PXT002331	-	mGluR4 modulator	Domain Therapeutics/Prexton Therapeutics	Parkinson's disease

A phase III study of NFC-1 in patients 6-12 years old with ADHD will start in the second half of 2017. Jefferies analysts note that phase III studies are expected to also include mutation-negative patients.

Clinical development targeting mGluR has suffered numerous setbacks in the past owing to safety and efficacy concerns. Little has progressed since *EP Vantage* last delved into the class back in 2009, and according to *EvaluatePharma* NFC-1 is the most advanced in the space *(Therapeutic focus – Addex could be leading the mGluR pack, November 17, 2009).*

Whether targeting a specific subpopulation can overcome the issues is still to be determined.

Project	**Setting**	**Trial ID**
bb2121	50 multiple myeloma pts	NCT02658929
NFC-1	Saga trial, 90 patients with mGluR+ ADHD	NCT02777931

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