Evaluate Vantage

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Snippet roundup: Immuno-oncology hopes for Parkinson's class, Coherus climbs

Edwin Elmhirst

Welcome to your weekly roundup of *EP Vantage*'s snippets – short takes on smaller news items.

This week, 11-15 July, we had thought on the following events: A2A inhibitors – not just for Parkinson's disease any more; a new immuno-oncology focus has emerged; Santhera joins its Duchenne rivals in US purgatory; Pharming goes up against Shire in HAE battle; Coherus rises sharply on biosimilar hopes; next round of sarcoma events after CytRx failure; Diurnal on track for 2018 European launch; will Ono be the boost Celyad needs as Juno setback raises concerns over CD19 CAR-T?

A2A inhibitors – not just for Parkinson's disease any more. A new immuno-oncology focus has emerged

15 July 2016

Juno Therapeutics' decision to acquire RedoxTherapies for $10m up front to secure rights to the adenosine A2A receptor antagonist vipadenant has probably raised a few eyebrows given that this class has struggled to make headway in central nervous system disease. However, the company is looking at the project as a potential modulator of immune suppression in cancer patients in the hopes of augmenting the tumour-fighting effects of its CAR-T candidates. Although most of the research in A2A has been in Parkinson's disease, a small immuno-oncology pipeline is now emerging, led by Corvus Pharmaceuticals' CPI-444, which is being tested in phase I as a monotherapy and with Roche's PD-L1 inhibitor Tecentriq. Most recently, AstraZeneca dosed the first patient in a phase I trial of HTL1071, from Sosei's Heptares Therapeutics subsidiary, as a monotherapy and in combination with its PD-L1 durvalumab.

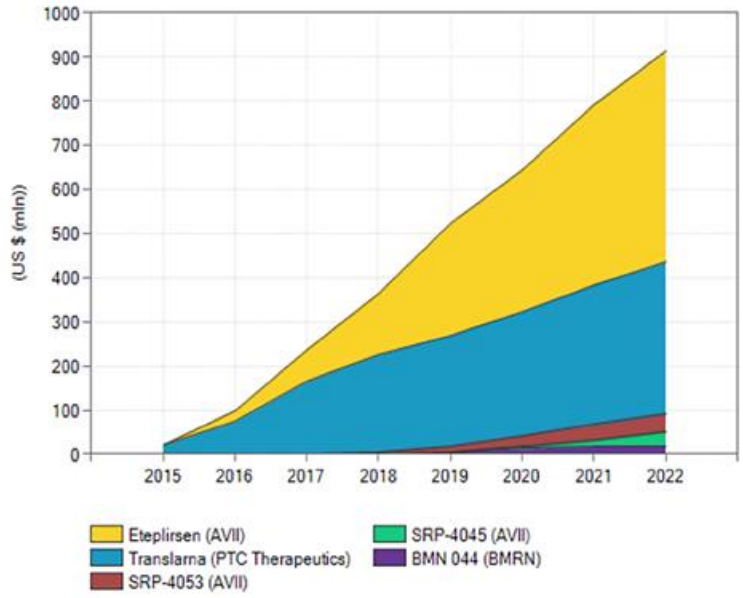
Adenosine A2A receptor antagonists in oncology

	Product	Company
Phase I	CPI-444	Corvus Pharmaceuticals
	HTL-1071 (AZD4635)	AstraZeneca/Sosei
Pre-clinical	V2006 (vipadenant)	Juno
Research project	GBV2034	Globavir

Santhera joins its Duchenne rivals in US purgatory

14 July 2016

The US FDA has made it abundantly clear that it won't cut corners in approving Duchenne muscular dystrophy drugs, and today Santhera became the latest victim of this tough stance. Its stock is trading down 40% after the agency said it wanted to see results of the Sideros trial before approving Raxone, and not on a confirmatory basis afterwards, as Santhera had hoped. This came after a refuse-to-file letter on PTC Therapeutics' Translarna, complete response letter for Biomarin's Kyndrisa and negative adcom vote on Sarepta's eteplirsen. With Sideros results not due until late 2019 it is possible – though not at all certain – that Raxone's delay until at least 2020 might give Santhera's rivals an advantage.



Pharming goes up against Shire in HAE battle

14 July 2016

Pharming faces the task of marketing its hereditary angioedema drug Ruconest alone in 21 additional countries after scaling back its partnership with Sobi. The Dutch group will be up against fierce competition, with six other drugs already approved for HAE and several more in development – including Shire's lanadelumab, forecast to be the top seller by 2022. Ruconest, meanwhile, is forecast to sell $10m. In the US, Pharming can still count Valeant as a partner, through its acquisition of Salix, but Ruconest seems unlikely to make its list of priorities.

Top-five hereditary angioedema drugs in 2022

Product	Company	Status	2022e sales ($m)
Lanadelumab	Shire	Phase III	1043
Cinryze	Shire	Marketed	615
Firazyr	Shire	Marketed	315
Avoralstat	BioCryst Pharmaceuticals	Phase III	98
Kalbitor	Shire	Marketed	80

Coherus rises sharply on biosimilar hopes

12 July 2016

Usually reporting phase I pharmacokinetic and pharmacodynamic results for a product is a non-event. But judging by the 33% jump in Coherus BioScience shares its investors are betting that the company will succeed in carving out decent US sales for CHS-1701, its biosimilar version of Amgen's Neulasta. This hope could be based on speculation that the relative simplicity of Neulasta might limit clinical requirements for biosimilar approval to just pharmacokinetics, pharmacodynamics and immunogenicity. Even if the bar is set higher Coherus has at least cleared one hurdle, meaning that there could be upgrades to current CHS-1701 forecasts. But carving out market share will not be easy as there are several other players going after the $4.72bn in sales Neulasta notched up last year. Bernstein analysts see up to seven companies poised to enter the US and EU markets by the end of 2017.

Coherus BioSciences top 2022 products

Product	Therapeutic Subcategory	2022e Sales ($m)	Current Market Status
Adalimumab	Immunosuppressants	236	Phase III
CHS-1701	Immunostimulants	199	Phase I

Next round of sarcoma events after CytRx failure

12 July 2016

CytRx shares are expected to plummet during in-market trading today after the California-based group said its "better chemotherapy" aldoxorubicin failed to improve survival in soft tissue sarcoma (STS) patients above that seen with standard treatments in a second-line setting. Novartis's Votrient is the biggest seller in STS, and is used in the relapsed/refractory setting after treatment with an anthracycline-based first-line treatment, and PharmaMar's Yondelis is used in the same setting in the EU. The sector is awaiting news on an FDA decision on

Lilly’s olaratumab, which could alter the STS treatment landscape if it receives approval in a first-line setting. The following candidates could have data in coming months.

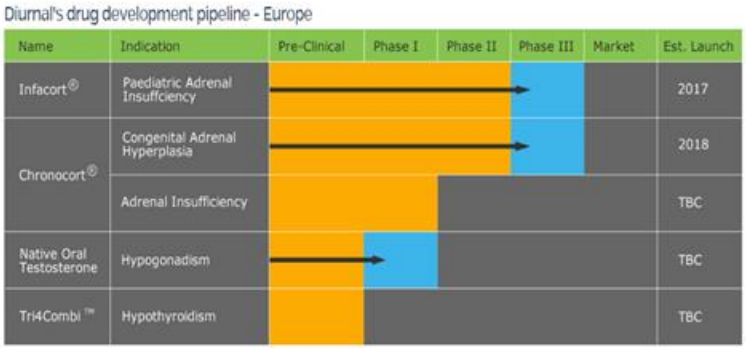
Selected soft-tissue sarcoma projects

	Product	Company	Pharmacological class
Filed	Olaratumab	Eli Lilly	Anti-platelet-derived growth factor (PDGFR)-alpha MAb
Phase III	Selinexor	Karyopharm Therapeutics	Exportin 1/chromosome region maintenance protein 1 (XPO1/CRM1) inhibitor
	Anlotinib Hydrochloride	Sino Biopharmaceutical	VEGFr2 & VEGFr3 kinase inhibitor
Phase II	CMB305	Immune Design	Cancer Vaccine
	Tecentriq	Roche	Anti-programmed death-1 ligand-1 (PD-L1) MAb
	Ontuxizumab	Eisai	Anti-tumor endothelial marker-1 (TEM-1) MAb

Diurnal on track for 2018 European launch

11 July 2016

In publishing positive phase three data for its paediatric adrenal insufficiency product, Infacort, Diurnal moves one step closer to launching the treatment for congenital adrenal hyperplasia (CAH) in Europe by 2018. If this regulatory hurdle is cleared preparations will begin for the EU launch of the orphan drug Chronocort, for adult CAH sufferers. Phase III results are expected by early 2018, and if positive could see a 2018 European launch. Analysts at Numis expect Diurnal shares eventually to hit 550-600p, a big jump from 144p when the group floated on London’s Aim last December, raising £30m ($44.7m). But, as Numis points out, this will depend on Chronocort unseating the current standard of care. As Diurnal is planning on launching alone, the next announcement is likely to be a capital raise to fund its ambitions.



Will Ono be the boost Celyad needs as Juno setback raises concerns over CD19 CAR-T?

11 July 2016

Celyad announced a licensing deal today with Ono Pharmaceutical for its tumour-targeting adaptive cell therapy using natural killer cell receptors. Celyad has dosed its autologous cell therapy in 10 patients at four different dose levels without reporting any adverse event signals, but trails more advanced projects from Novartis, Juno Therapeutics and Kite Pharma. A setback for Juno’s CD19-directed CAR-T announced last week could allow Celyad some time to catch up as the first wave of adoptive cell therapy projects take aim at the same target.

Six CAR-T clinical trials to watch

Source: EP Vantage and company filings

Project	Company	Study	Indication	Timeline	Trial ID
KTE-C19	Kite	Zuma-1	Non-Hodgkin's lymphoma; "pivotal" study	Interim data H2 2016; US filing 2016, US approval 2017	NCT02348216
CTL019	Novartis	Eliana	Paediatric ALL pts	US filing 2017	NCT02435849
JCAR015	Juno	Rocket	Adult ALL pts; "potentially registrational" study	US filing late 2017, US approval 2018	NCT02535364
JCAR017	Juno	–	Non-Hodgkin's lymphoma	US filing 2018	NCT02631044
CTL019	Novartis	Juliet	Diffuse large B-cell lymphoma	–	NCT02445248
KTE-C19	Kite	Zuma-3	Adult ALL pts	–	NCT02614066

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