

Upcoming events - Genmab's route to market, and late-stage data for Zogenix



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Genmab is seeking data to position tisotumab as its first in-house launch, while Zogenix wants Fintepla to challenge GW in Lennox-Gastaut syndrome.

Welcome to your weekly roundup of approaching clinical readouts. Genmab has some nice royalty generators in Darzalex, Arzerra and the just-approved Tepezza, but sells no drugs of its own – a situation that could change with the anti-tissue factor conjugate tisotumab vedotin.

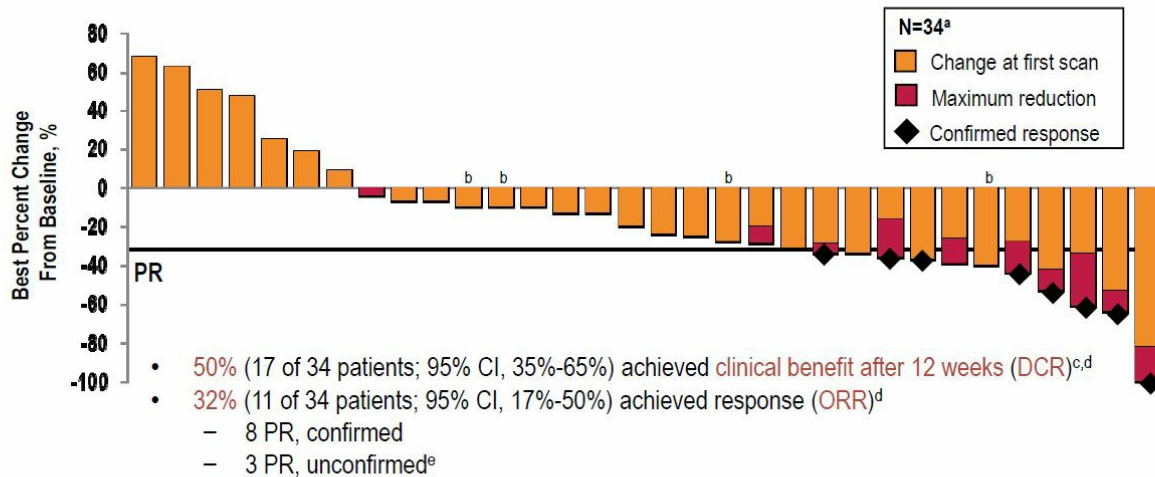
Before the middle of this year two studies testing tisotumab in cervical cancer will read out: [Innova-205](#), a first-line combo trial, and [Innova-204](#), a monotherapy test in previously treated subjects. The second is vital, as it could pave the way to a regulatory filing and a 2021 launch.

EvaluatePharma sellside consensus computes 2024 forecast revenues of \$241m for tisotumab, while Jefferies analysts cite the potential for \$600m of peak sales, half derived from cervical cancer.

Tisotumab has a curious history, having initially been in sole development by Genmab, based on antibody-drug conjugate technology licensed from Seattle Genetics. In 2017 Seattle saw enough potential to opt into a formal 50/50 cost and profit-sharing deal.

Innova-204 tests objective remission rate as primary endpoint, and investors can handicap the result, thanks to an earlier multi-tumour trial called GEN701.

32% OF PATIENTS WITH RECURRENT/ADVANCED CERVICAL CANCER ACHIEVED RESPONSE WITH TISOTUMAB VEDOTIN



CI=confidence interval; CR=complete response; CT=computed tomography; DCR=disease control rate; ORR=overall response rate; PD=progressive disease; PR=partial response; RECIST=Response Evaluation Criteria in Solid Tumors; SD=stable disease.

^aTwo patients were withdrawn prior to CT scan, and so are not represented in the graph. ^bPD due to new lesion at same scan. ^cClinical benefit was defined as the DCR rate, the proportion of patients who achieved a CR, PR, or SD after 12 weeks. ^dResponse was as assessed by investigators using standard RECIST 1.1 criteria. ^eOne of which is still ongoing. Data cutoff date July 24, 2017.

Remission rates in GEN701's cervical cancer cohort. Source: Dr Ignace Vergote & Esmo 2017.

Here, in 34 cervical cancer subjects, tisotumab achieved 11 responses (eight confirmed), including a 46% ORR in second-line and 36% in third-line disease. Conjunctivitis was the most frequent adverse event, though its rate at grade 3 or above was just 3%.

While paclitaxel/platinum/Avastin are a front-line cervical cancer standard, numerous therapies are used second line, including topotecan, Abraxane and other chemos, and these are associated with ORRs of 5-21%.

Innov-204 has a recruitment target of 102, and will surely struggle to replicate the 46% ORR of the GEN701 second-line cohort. Clearly, however, a number well above 20% is a must, and if this is hit Genmab could be on its way to market.

Zogenix looks to second place

This quarter Zogenix will report [phase III data for Fintepla](#) in Lennox-Gastaut syndrome, a severe form of epilepsy that begins in childhood. GW Pharma's Epidiolex gained approval in this condition in 2018, so Zogenix will need to better the cannabidiol to make up for its late showing to the market.

Epidiolex showed a [median 22% to 25% placebo-adjusted reduction](#) from baseline in frequency of drop seizures at its highest dose, 20mg/kg/day. Zogenix's trial has the same primary endpoint and is testing two doses, 0.2mg/kg/day or 0.8mg/kg/day, versus placebo in 225 patients on a background therapy of anti-epileptics.

In an [earlier single-arm study](#) Fintepla showed a median [50% reduction in seizure frequency](#) over 20 weeks versus baseline, albeit in just 13 subjects. To be best in class Fintepla will also need to beat some older anti-epileptics approved for Lennox-Gastaut, and Leerink analysts say it needs to be in at least the 50% range of placebo-adjusted improvement.

The older drugs come with a range of side effects and black box warnings, but Fintepla has had a relatively clean safety profile across late-stage trials in another type of intractable epilepsy called Dravet syndrome, for which it is filed.

No serious cardiovascular issues have been observed - a crucial point, as Fintepla's active ingredient is flenfluramine, half of the "fen-phen" diet pill that was found to cause serious heart problems.

GW's Epidiolex has shown elevations of liver enzymes at high doses, but these are said to be manageable. Epidiolex is expected to lead the Lennox-Gastaut market by 2024, according to *EvaluatePharma* consensus forecasts, but Fintepla has a shot at second place.

Biggest-selling Lennox-Gastaut treatments

Product	Company	Mechanism	Indication sales (\$m)		Indication status
			2020e	2024e	
Epidiolex	GW Pharmaceuticals	Cannabinoid receptor agonist	238	538	Marketed
Fintepla	Zogenix	Selective 5-HT reuptake inhibitor; Sigma-1 opioid receptor regulator	-	374	Phase III
Klonopin	Roche	GABA A receptor agonist	143	127	Marketed
Banzel	Eisai	Sodium channel blocker	191	120	Marketed
Sympazan	Aquestive Therapeutics	GABA A receptor agonist	16	66	Marketed

Source: EvaluatePharma.