Evaluate Vantage

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Upcoming events – Phase III readouts loom for Urogen and Mediwound

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Urogen is gearing up to release the results of a pivotal trial of its lead asset – and so is Mediwound.

Welcome to your weekly digest of approaching regulatory and clinical readouts. Urogen hopes to start 2019 with a strong readout from a pivotal trial of its lead asset, UGN-101; topline data from a study called Olympus are due in January.

UGN-101 is a slow-release gel formulation of the chemotherapy agent mitomycin. The company is trying to show that it can ablate non-invasive tumours without the need for radical or repeated surgery; its lead indication is low-grade upper tract urothelial cancer (UTUC), while work in low-grade bladder cancer is not too far behind.

There are no drugs approved to treat UTUC specifically. It is hard to get to these tumours, so the entire kidney and upper urothelial tract often have to be removed. Success in the Olympus study could mean that UGN-101 is approved as a first-line chemoablation treatment.

Olympus is 90% powered to show that the observed complete response rate is superior to 15%, the primary endpoint of the study. Interim analyses of the open-label, single-arm trial suggest that this should be hit easily; back in May Urogen presented a complete response rate of 59% from 34 evaluable subjects.

Around 70 patients are to be recruited; durability of response is a key secondary endpoint, though this is unlikely to be mature for the January cut. Full data are to be presented in the second quarter.

Urogen intends to start a rolling US NDA early next year, and could also begin talking to the regulator about moving forward in bladder cancer. A phase II study in this setting is to read out in the first half of 2019.

Sick burns

Meanwhile, for Mediwound topline data from a US phase III trial of the burn debridement product NexoBrid are due in the coming weeks.

The 175-patient Detect trial evaluates the ability of NexoBrid, also a gel formulation but this time composed of several proteolytic enzymes including bromelain, to remove eschar, the dead tissue that surrounds burns.

Detect’s primary endpoint, rate of complete eschar removal, compares NexoBrid against gel vehicle. It is only

the secondary endpoints – rates of surgery, duration until eschar removal and blood loss – that will be measured against investigator's choice standard of care, a combination of surgical and non-surgical eschar removal procedures.

In its European phase III study the incidence of successful eschar removal with NexoBrid was 96.3% versus 0% with vehicle. Rates of surgical removal of tissue was 24.5% in the NexoBrid group versus 70% among patients given standard of care. NexoBrid also allowed earlier eschar removal, at 2.2 days from injury versus 8.7 days with standard treatment.

The EMA, which approved NexoBrid in 2012, says 15% of the wounds treated with NexoBrid required surgery to remove the eschar compared with 63% treated with standard care. Around 18% of wounds required a skin graft, compared with 34% with standard treatment.

This level of performance was good enough for the EU regulator, so presumably the FDA will be satisfied with similar results from Detect. The question is whether the US agency will allow a BLA filing based on these interim data or if it will wait for longer-term endpoints, which concern scarring and quality of life. Approval could come in late 2020 at the earliest.

But the stakes are higher than just NexoBrid's approval. The drug is Mediwound's lead product, and the follow-up, EscharEx, contains the same enzyme mixture as NexoBrid but is geared towards chronic and other hard-to-heal wounds. Failure of one would likely mean failure of the other.

Mediwound's forecast sales

		Global sales ($m)				
Product	**Status**	**2018e**	**2020e**	**2022e**	**2024e**	**CAGR**
NexoBrid	Marketed	4	15	36	71	+65%
EscharEx	Phase II	-	1	5	31	n/a
Total		*4*	*15*	*41*	*103*	*+75%*

Source: EvaluatePharma.