Evaluate Vantage

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Upcoming events – Milestone's milestone and Transmedics' panel

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Soon Milestone will report pivotal data with etripamil, an intranasal heart arrhythmia therapy, and an FDA adcom approaches for Transmedics' heart preservation system.

Welcome to your weekly roundup of approaching clinical and regulatory readouts. The pivotal trial of Milestone Pharmaceuticals' only clinical product, the intranasal calcium channel blocker etripamil, will report by the end of March. The Node-301 study is in 500 patients with paroxysmal supraventricular tachycardia (PSVT) – sudden and unexpected episodes of rapid heart rate.

PSVT isn't typically life-threatening but episodes can last from minutes to hours and are associated with chest pain, fatigue and fainting. According to Milestone, patients with PSVT experience a median of four to seven episodes per year, despite up to two-thirds of them taking medications. Etripamil is intended for episodic use. Milestone notes that current options for this type of treatment are intravenous calcium channel blockers, so etripamil needs to play the convenience card.

In Node-301 adult patients are randomised to receive either 70mg etripamil as a self-administered nasal spray or placebo. The primary endpoint is time to conversion to normal sinus rhythm.

Just a single efficacy trial is needed to support NDA submission. But two open-label safety studies, Node-302 and Node-303, are needed to support an FDA-required safety database of around 1,500 unique PSVT patient events. Both safety studies have a primary completion date next year.

In the dose-ranging Phase II Node-1 study, 70mg etripamil converted 87% of PSVT patients to normal sinus rhythm within 15 minutes, versus only 35% for placebo, without a drop in blood pressure, the difference was statistically significant.

Etripamil's 2024 sales are forecast to reach $92m according to *EvaluatePharma* consensus, with an NPV of $427m, just over the company's $423m market cap. Milestone completed its $95m IPO last year and shares are down 4% to date. The company has $120m in cash, which is expected to last into the third quarter of next year.

Take heart

With shares in Transmedics having lost a quarter of their value since the company floated last May, the group

could do with some good news to stem the bleeding. An upcoming FDA adcom could supply a bit of uplift, should it go well.

Assuming it is not called off owing to the Covid-19 pandemic, the FDA's circulatory system devices panel will meet on April 16 to discuss the approvability of Transmedics' Organ Care System (OCS) Heart. The device is designed to preserve a donated heart outside the body for transplant into a patient by keeping it warm and beating, and in a metabolically active state. Its monitoring capabilities allow physicians to judge a potentially suitable heart's condition and viability.

The device's development in the US lags its European status significantly: OCS Heart was originally CE marked in September 2006. The UK's Nice guidelines state that the system can extend preservation times compared with cold storage for hearts donated after brainstem death.

In the pivotal US-based Expand Heart trial, 75 of 93 donor hearts assessed using Transmedics' machine were successfully transplanted, giving a utilisation rate of 81%. In the 75 transplanted patients, 30-day survival was 95%. The donor hearts in the trial would not have been suitable for use had they been preserved with cold storage, suggesting that using OCS Heart can improve the desperately limited supply of donor hearts.

A version of the OCS designed to preserve human lungs for transplant was approved in the US two years ago. Transmedics is also developing a version for donor livers.

Trials of OCS-Heart

Name	ID	N	Details	Results
Proceed II	NCT00855712	128	Vs cold storage, endpoint survival 30 days post-transplant	Non-inferior to cold storage
Expand Heart	NCT02323321	75	Single-arm, endpoint survival 30 days post-transplant	Permitted use of donor hearts unsuitable for cold storage
Expand Heart CAP	NCT03835754	48	Single-arm, endpoint survival 30 days post-transplant	Late 2020
DCD-Heart	NCT03831048	212	Vs cold storage, endpoint survival six months post-transplant	Late 2021

CAP = continued access protocol. Source: EvaluateMedTech, clinicaltrials.gov.