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Five Pivotal Trial Read-Outs To Look Out For In Early 2022

by Ayisha Sharma

Five notable studies are expected to report top-line data in the first quarter. With the help of Biomedtracker's Early 2022 Outlook Report, we take a look at the major catalysts likely to kick off the year, including in heart failure and wet AMD.

Cytokinetics' Omecamtiv For Heart Failure

Cytokinetics, Inc. is expected to release top-line data from the Phase III METEORIC-HF study of omecamtiv mecarbil, a selective cardiac myosin activator, by the end of April. The METEORIC-HF study has enrolled 276 heart failure patients with reduced ejection fraction and decreased exercise tolerance and measures the primary endpoint of change in peak oxygen uptake on cardiopulmonary exercise testing from baseline to week 20.

The development of omecamtiv has been hindered by obstacles, with the candidate showing only a slim efficacy benefit in the much-anticipated Phase III GALACTIC-HF trial composite primary endpoint and missing all secondary endpoints. (Also see "*Cytokinetics Sees Omecamtiv Potential In Certain Heart Failure Patients*" - Scrip, 13 Nov, 2020.) The lukewarm data prompted former partner Amgen to return its rights to the drug to Cytokinetics in 2020 following a deal first inked in 2006. (Also see "*Amgen Hands Omecamtiv Back To Cytokinetics*" - Scrip, 23 Nov, 2020.)

However, Merck's rival Verquvo (vericiguat), a soluble guanylate cyclase stimulator, won US Food and Drug Administration last year for a similar population with a comparatively modest benefit, analysts at Biomedtracker noted. (Also see "*Merck & Co. Pushes Back On Modest Projections For Verquvo*" - Scrip, 20 Jan, 2021.) Besides, since exercise capacity is rarely evaluated, positive results from the METEORIC-HF trial could offer differentiating factor for omecamtiv over its competitors, they added.

Cytokinetics lisenced the Chinese rights for omecamtiv to *Ji Xing Pharmaceuticals* at the end of last year, expanding upon an existing collaboration with the biotech. (Also see "*Asia Deal Watch:*

Cytokinetics Licenses China Rights For Omecamtiv To Ji Xing" - Scrip, 21 Dec, 2021.)

Ascendis' TransCon PTH For Hypoparathyroidism

Topline data from the Phase Phase III PaTHway study of *Ascendis Pharma A/S*'s TransCon PTH in adult patients with the rare disease hypoparathyroidism (HP) are anticipated by the end of March. TransCon PTH is a prodrug of parathyroid hormone (PTH) that aims to restore PTH levels for 24 hours every day to normalize blood and urinary calcium levels, serum phosphate levels and bone turnover.

The PaTHway study completed enrolment of 82 patients in May last year and measures proportion of subjects with albumin-adjusted serum calcium within the normal range who are independent form active vitamin D and therapeutic doses of calcium as a primary endpoint. Data from the trial could support a new drug application with the FDA planned for the third quarter of this year. The Danish firm is also planning pediatric studies for the asset.

Ascendis' candidate is the most advanced one in the clinic for HP, followed by *BridgeBio Pharma, Inc.*'s calcium-sensing receptor antagonist encaleret and *Entera Bio Ltd.*'s oral formulation of teriparatide (a recombinant form of PTH), both at Phase II development. Furthermore, past results for TransCon PTH were promising, analysts at Biomedtracker noted. Updated data from week 84 of the Phase II PaTH Forward study showed 93% of treated subjects were free from taking active vitamin D and took less than 600mg of calcium per day.

Embera's EMB-001 For Smoking Cessation

Embera NeuroTherapeutics, Inc.' topline Phase II/III data for its smoking cessation candidate EMB-001 are expected by the end of March. The oral asset is a combination of two FDA-approved drugs, the cortisol synthesis inhibitor metyrapone and the short-to-medium acting benzodiazepine oxazepam.

Given its differentiated mechanism from existing addiction treatment options, EMB-001 could prove a meaningful addition to the smoking cessation market which sees 75% of patients resume smoking within a year. The candidate could also be used in conjunction with approved therapies, analysts at Biomedtracker noted.

Embera is currently recruiting between 25 and 50 subjects for a Phase IIa study initiated in May last year. The primary endpoints are smoking abstinence at weeks nine through 12, week 12 and at a six-month follow-up. Investors in the private company took part in a $1.3m financing to support the study. The Boston, MA-based biotech first funded a Phase I dose-ranging study for the candidate with $2m raised in the second part of its series A financing in 2015. SC028401

The biotech has also initiated a Phase II study for EMB-001 in cocaine use disorder, topline results from which are expected in the first quarter of this year. Over 70% of the target enrolment

of 80 patients had been recruited in June last year.

As for the competition, notable big pharma candidates in the addiction space include *Novartis AG*'s Phase II oral metabotropic glutamate receptor 5 antagonist, mavoglurant, for cocaine use disorder and *AstraZeneca PLC*'s Phase I orexin 1 antagonist for smoking cessation.

Arena's Etrasimod For Ulcerative Colitis

Arena Pharmaceuticals, Inc. has changed tack after its S1P receptor modulator and lead candidate etrasimod flunked an atopic dermatitis study in 2020 with a renewed focus on ulcerative colitis (UC). (Also see "*Arena Sees Phase III Path For Etrasimod After Atopic Dermatitis Miss*" - Scrip, 10 Nov, 2020.) Data from a Phase II etrasimod study in severe UC showed that patients receiving the 2mg dose achieved significant improvements versus placebo in the primary, all secondary, and clinical remission endpoints.

Now, attention turns to topline results from the Phase III ELEVATE UC 52 trial, which are anticipated by the end of March. The ELEVATE UC 52 study was initiated in 2019 while another Phase III study, ELEVATE UC 12, started in 2020. More than 700 patients with moderately to severely active UC have been enrolled across both trials.

ELEVATE UC 52's coprimary endpoints measure the proportion of participants achieving clinical remission assessed by Mayo component sub-scores at 12 weeks and 52 weeks. Etrasimod is the most advanced S1P agonist in the clinic for UC, followed closely by *Ventyx Biosciences, Inc.*'s VTX-002 and *Biogen, Inc.*'s amiselimod, both at Phase II.

Arena was recently acquired by *Pfizer Inc.* in a deal worth $6.7bn as part of the major's strategy to diversify its inflammation and immunology pipeline. (Also see "*Pfizer Buys Arena For $6.7bn In Bid To Diversify In Inflammation & Immunology*" - Scrip, 13 Dec, 2021.)

Kodiak's KSI-301 For Wet AMD

Lastly, *Kodiak Sciences Inc.* is expected to announce topline data from the Phase IIb/III DAZZLE study of its vascular endothelial growth factor (VEGF) receptor antagonist KSI-301 (tarcocimab tedromer) in wet age-related macular degeneration (wet AMD) by the end of April. The controlled study compares Kodiak's lead asset with *Regeneron Pharmaceuticals, Inc.*'s standard of care Eylea (aflibercept) in treatment-naive wet AMD.

Kodiak reported preliminary results from a Phase Ib study in wet AMD, diabetic macular edema and retinal vein occlusion, showing strong improvements in vision and retinal anatomy were observed over 12 weeks and detected signs of disease modification. Notably, there were no intraocular inflammation (IOI) or ocular serious adverse events reported after 200 injections. The lack of IOI as a contraindication could give Kodiak's asset an edge over competitors if approved by the FDA, the Biomedtracker analysts noted.

However, Kodiak faces tough competition, as there are 35 other VEGF receptor antagonists in the clinic for wet AMD, according to the Citeline database Pharmaprojects. Elsewhere in the wet AMD pipeline, rival *Roche Holding AG*'s anti-VEGF bi-specific antibody faricimab has produced filing-worthy Phase III data but has shown no advantage over Eylea. (Also see "*Roche Prepares Faricimab For Filing After Phase III AMD Data*" - Scrip, 26 Jan, 2021.)

For more information, see Biomedtracker's *Early 2022 Outlook Report*.

Wet AMD Market Snapshot: A High-Growth Market Poised For Change

By Jessica Merrill

17 Sep 2021

Regeneron's Eylea and Roche's Lucentis currently dominate the treatment market for wet-AMD and diabetic eye disease, but biosimilar ranibizumab and new brand launches are on the horizon.

Read the full article here

Editor's Note: This article has been updated to correct the spelling of omecamtiv mecarbil.