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Top 10 Things To Watch For At DDW

by David Wild

At Digestive Disease Week, Celltrion will seek to strengthen its hold on the IBD market, Ironwood hopes to expand Linzess into pediatric functional constipation, and competitors will showcase competing short bowel syndrome treatment and colorectal cancer companion diagnostics.

Biopharmas large and small will try to make headway into a variety of markets and solidify or expand their foothold in existing markets at this year's Digestive Disease Week, to be held in Chicago 6-9 May. Here are 10 developments we'll be watching for in our on-site coverage:

#1: Inflammatory Bowel Disease

Celltrion USA will present five analyses focusing on use of its subcutaneous version of Remsima (infliximab-dyyb) in inflammatory bowel disease. The Phase III LIBERTY-UC and LIBERTY-CD studies—in ulcerative colitis and Crohn's disease, respectively—both compared the formulation's use as maintenance therapy to subcutaneous placebo in patients who received open-label induction therapy with intravenous Remsima.

The LIBERTY studies will also be included in two larger analyses: a comparative analysis looking at efficacy-related treatment discontinuation rates among UC patients given subcutaneous or intravenous Remsima and *Takeda Pharmaceutical Co. Ltd.*'s Entyvio (vedolizumab); and a meta-analysis comparing the efficacy of I.V. or SC infliximab and Entyvio as maintenance in adults with UC or CD.

These data may be just the kind of "new clinical information" Celltrion's US chief commercial officer Thomas Nusbickel told *Scrip* he hopes will encourage uptake of the subcutaneous Remsima, which is approved in the EU, Korea and Canada and could receive US regulatory approval in the second half of 2023. (Also see "*Celltrion CCO On The Big US Build-Up, Direct Sales Model*" - Scrip, 26 Apr, 2023.)

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Janssen will also be presenting the first Phase III readout from the QUASAR induction study. The study is looking at Tremfya (guselkumab), the company's fully humanized IgG1 monoclonal antibody targeting the p19 subunit of IL-23, in adults with moderately-to-severely active ulcerative colitis refractory to other treatments. A prior Phase IIb/III efficacy readout from QUASAR pointed to best-in-class potential, showing an 80% clinical response at week 12 or 24. Tremfya is approved for subsets of patients with moderate-to-severe plaque psoriasis and for adults with active psoriatic arthritis. The drug brought in $640m in the first quarter, and a possible expansion to the UC population would be an important boon, as Stelara (ustekinumab) loses patent exclusivity this year.

#2: *Clostridioides Difficile* Infection

On the heels of US approval of *Seres Therapeutics, Inc.*'s oral microbiome therapy, Vowst (formerly SER-109), for the prevention of recurrence of *C. difficile* infection (CDI) in adults after antibacterial treatment for recurrent CDI, *Ferring Pharmaceuticals* will present several datasets focused on the safety and efficacy of its rival product, Rebyota, including in immunocompromised patients and those with inflammatory bowel disease.

Approved in December 2022, Rebyota has first-to-market advantage, but whether it can maintain its foothold with the entry of Vowst remains to be seen. One of the main differentiators is that Rebyota is a one-time, rectally-administered treatment administered by a physician, while Vowst is given as four pills for three consecutive days. Cost and reimbursement will also be keys to determining uptake.

However, both treatments may ultimately lose ground to other companies developing microbiome-targeting CDI treatments that do not need donor-derived feces and thus avoid concerns surrounding pathogen transmission that accompany donor-derived feces. (Also see "*CDI Market Snapshot: Microbiome Therapies Begin Descent On Landscape*" - In Vivo, 19 Dec, 2022.)

#3: Functional Constipation

Ironwood Pharmaceuticals, Inc. is set to expand its functional constipation (FC) indication for Linzess (linaclotide) to patients less than 18 years of age. The FDA is reviewing a claim for use in children and adolescents ages 6-17 years of age with FC with a 14 June user fee date.

The pivotal Phase III data being presented at DDW in this population will clarify how successful it is in expanding use to the six million young people in the US living with FC. The drug is currently approved in the US for adults with irritable bowel syndrome with constipation (IBS-C) as well as for adults with chronic idiopathic constipation.

Ironwood's partner, *AbbVie Inc.*, reported first quarter sales of $251m for Linzess, a 7.7% year-

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over-year increase.

#4 and #5: Liquid Biopsies For Colorectal Cancer

InterVenn Biosciences and *Guardant Health, Inc.* are trying to make inroads into the lucrative companion diagnostics market. Both will be presenting data on their respective liquid biopsy assays for the detection of early-stage colorectal cancer (CRC).

InterVenn Biosciences's poster is expected to provide evidence their platform can detect not only CRC, but advanced adenomas, which are precursors to cancer and thus present an important screening target for clinicians. Their GlycoVision platform relies on measurements of circulating serum glycoproteins, unlike other liquid biopsies for CRC that primarily rely on circulating tumor DNA (ctDNA).

Guardant Health, Inc.'s Shield is one of the tests that use ctDNA, and the company will be presenting two sets of data, including a late-breaker of its ECLIPSE study, highlighting the test's ability to screen for early-stage CRC. Shield is currently available as a laboratory developed test (LDT) in the US, but the DDW data will support its premarket approval (PMA) submission to the FDA for the detection of colorectal neoplasia.

Preliminary results from ECLIPSE, which includes a demographically diverse US population of over 20,000 average-risk adults 45-84 years of age, showed an impressive 83% sensitivity and 90% specificity in detecting CRC. However, the company will want to show Shield can also accurately detect advanced adenomas, as InterVenn Biosciences could emphasize in its data.

#6 and #7: Short Bowel Syndrome

VectivBio Holding AG is presenting data from its Phase II STARS Nutrition study, looking at its next-generation, long-acting GLP-2 analog, apraglutide, for patients with short bowel syndrome colon-in-continuity (SBC-CIC). Top-line results from the study presented in 2022 indicated it can significantly reduce parenteral support needs in these patients.

The company's stock shot up recently due to enthusiasm about those data and about the Phase III STARS study, which is expected to confirm later this year that the drug can reach study outcomes in patients with SBS-intestinal failure (SBS-IF) as well.

Zealand Pharma A/S is also vying for a spot in the SBS market with their own long-acting GLP-2 analog, glepaglutide. The company is expected to submit glepaglutide, which is administered via autoinjector, to the FDA for the SBS indication in the second half of 2023. Citeline analysts noted top-line results from the Phase III EASE SBS-1 Study of glepaglutide were mixed, showing only

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patients receiving the twice-weekly dose achieved the primary endpoint of absolute change in weekly parenteral support volume.

Ease of administration could be the key differentiator between once-weekly apraglutide, possibly twice-weekly glepaglutide and Takeda Pharmaceutical Co. Ltd.'s once-daily Gattex (teduglutide), the only GLP-2 approved for SBS, which brought in $675m in revenue for the Japanese pharma in 2021. (SC147203)

#8: Exocrine Pancreatic Insufficiency

First Wave BioPharma, Inc. will present Phase II dose-escalation data on adrupilase, its candidate for patients with cystic fibrosis (CF) and severe EPI. The company believes adrulipase has best-in-class potential for EPI associated with CF and for chronic pancreatitis (CP), both in combination with the current standard of care, porcine-derived pancreatic enzyme replacement therapy (PERT), and, importantly, as a monotherapy. More than 30,000 patients in the US have EPI caused by CF and approximately 90,000 have EPI caused by CP.

#9: Gastroparesis

Evoke Pharma, Inc. will be offering real-world evidence it hopes will increase uptake of Gimoti, its approved metoclopramide nasal spray, in patients with acute and recurrent diabetic gastroparesis. The health care utilization study will compare visits to physicians' offices, emergency rooms, and inpatient and outpatient hospital stays with oral and nasal metoclopramide.

According to the company, nasal administration overcomes the challenge of "erratic" gastric emptying in gastroparesis patients and related unpredictable oral medication absorption. Gimoti was approved in June 2020 and, according to Biomedtracker, sales in the US have increased from $2m in 2021 to $16m in 2022 during that time.

Safety controversies have plagued the gastroparesis space. *Janssen Pharmaceutica Inc.* withdrew its prokinetic Propulsid (cisapride) in 2000 and the only other FDA-approved gastroparesis therapy – *ANI Pharmaceuticals, Inc.*'s oral metoclopramide, Reglan – carries restrictive safety labeling. (Also see "*Teva Concedes On US Gimoti ANDA, Voiding 180-Day Exclusivity*" - Generics Bulletin, 2 Feb, 2023.)

#10: Celiac Disease

New York City-based *Immunic Inc* will showcase early data from a Phase I study of its celiac

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disease candidate, IMU-856. The oral agent is meant to improve intestinal barrier function and help regenerate bowel epithelium and was found in preclinical studies to avoid immune suppression. It can potentially be used in other conditions featuring impaired intestinal barrier function.

While it's early days for the agent, the data could attract investors to help the company fund expensive studies for both IMU-856 and other pipeline products, like its lead asset, vidofludimus calcium, for ulcerative colitis. (Also see "*Immunic Doubles Down On Lead Asset With New Data In Ulcerative Colitis*" - Scrip, 5 Apr, 2023.)

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