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Deal Watch: OrsoBio Reveals Its Metabolic Health Focus With Four Licensing Pacts

by Joseph Haas

California biotech also notes prior licensing deal with Gilead for mitochondrial candidate. Twentyeight-Seven acquires RNA-splicing cancer candidate from Basilea.

Scrip regularly covers business development and deal making in the biopharmaceutical industry. Deal Watch is supported by deal intelligence from Biomedtracker.

OrsoBio Splurges With Four Concurrent Licensing Transactions

Metabolic disease-focused *OrsoBio, Inc.* made a splash on 2 November by unveiling licensing agreements with three biopharmas as well as a fourth with *Yale University*. Based in Palo Alto, CA, the company got its start in 2020 with a previously undisclosed in-licensing from *Gilead Sciences, Inc.* of TLC-6740, a preclinical liver-targeted mitochondrial protonophore, as well as a library of mitochondrial protonophores and associated intellectual property.

The company acquired an ACMSD (alpha-amino-beta-carboxy-muconate-semialdehyde decarboxylase) inhibitor program from *Astellas Pharma, Inc.* subsidiary *Mitobridge, Inc.*, comprising a range of compounds that may be able to address mitochondrial dysfunction in metabolic and inflammatory liver and kidney disorders. OrsoBio said it has made chemistry and pharmacology progress in characterizing the biological effects of these compounds, and exploring complementarity with other pipeline programs.

ACMSD is highly expressed in the liver and kidneys, with the result of reducing NAD+ (nicotinamide adenine dinucleotide) in patients with advanced hepatic and renal disease. Preclinical TLC-065 and other compounds within the ACMSD inhibitor portfolio are being studied for their potential to replenish NAD+ and improve mitochondrial function, OrsoBio noted.

The biotech also obtained worldwide rights to an ACC2 (acetyl-CoA carboxylase 2) inhibitor program from *Shionogi & Co. Ltd.*, including lead candidate TLC-3595 (formerly S-723595), which is designed to treat type 2 diabetes by increasing fatty acid oxidation (FAO), reducing ectopic lipid accumulation and improving insulin sensitivity in skeletal muscle and liver. Initiation of a Phase IIa trial of TLC-3595 in subjects with insulin resistance is expected during H1 2023. OrsoBio said the candidate also may offer potential in other FAO-impairment conditions such as sarcopenia.

In addition, OrsoBio acquired assets relating to the liver X receptor (LXR) inverse agonist program from *Phenex Pharmaceuticals AG*, including lead candidate TLC-2716 and associated intellectual property. TLC-2716 has demonstrated potent and consistent effects to improve circulating plasma triglycerides and cholesterol and to reduce hepatic steatosis in preclinical models, the company said. A Phase I study of TLC-2716 for the treatment of severe dyslipidemias is expected in 2023.

In a separate concurrent deal, the firm in-licensed TLC-1235, a controlled-release mitochondrial protonophore from Yale.

Basilea Sells Off CLK Kinase Cancer Portfolio To Twentyeight-Seven

Switzerland's *Basilea Pharmaceutica Ltd.* out-licensed a portfolio of novel Cdc-2 like (CLK) kinase inhibitors on 2 November to *Twentyeight-Seven Therapeutics*, a biotech focused on RNA and DNA regulators. Under the agreement, Basilea gets CHF1m (about $1.01m) up front and could earn near-term milestones of CHF2m. In addition, Basilea could realize up to CHF351m tagged to development, regulatory and sales milestones.

Basilea said the deal will keep it on track with its stated intention to become a leading anti-infectives company, while divesting its oncology assets. By year's end, the company plans to have no material expenses related to oncology.

Agios Sells Tibsovo Royalties To Sagard Healthcare

Agios Pharmaceuticals, Inc. agreed on 27 October to sell its rights to 5% royalties on US net sales of *Les Laboratoires Servier*'s Tibsovo (ivosidenib tablets) to Sagard Healthcare Partners for a one-time payment of $131.8m. In September, Sagard paid $115m up front in exchange for global royalty rights to *Albireo Ltd.*'s Bylvay (odevixibat) for the rare cholestatic liver disease progressive familial intrahepatic cholestasis (PFIC). (Also see "*Deal Watch: Bristol Accesses Tech Platforms From SyntheX, Autolus*" - Scrip, 5 Oct, 2022.)

Tibsovo is a targeted therapy approved in the US to treat adult patients with an isocitrate dehydrogenase-1 (IDH1) mutation with acute myeloid leukemia (AML) or cholangiocarcinoma (bile duct cancer). Under a 2020 deal, Agios sold its oncology portfolio – including Tibsovo and the Phase III glioma candidate vorasidenib (AG-88) – to Servier. (Also see "*Agios Sells Cancer*

Portfolio To Servier To Focus On Genetic Diseases" - Scrip, 21 Dec, 2020.) Agios retains rights under the deal to a potential milestone payment of $200m for vorasidenib, as well as 15% royalties on US net sales of the drug.

Aquestive Licenses Lennox-Gastaut Therapy To Assertio Affiliate

Aquestive Therapeutics, Inc. inked a transaction on 27 October to license its Sympazan (clobazam) oral film to Otter Pharmaceuticals. Under the agreement, Aquestive will license the candidate and related intellectual property to the *Assertio Holdings, Inc.* subsidiary for $9m up front. Aquestive also will continue pursuing a patent application that could extend coverage for Sympazan to as late as 2039. The Warren, NJ-based firm will get a $6m milestone and royalty rights upon the patent allowance, Otter said.

Sympazan is intended as an adjunctive treatment for seizures associated with Lennox-Gastaut syndrome in patients aged two years of age or older. Aquestive also entered into a long-term supply agreement with Assertio for the product under the agreement.

Genmab Nabs Glycan-Targeted Antibody From Scancell

Genmab A/S obtained global development and commercial rights on 24 October an anti-glycan monoclonal antibody discovered by UK biopharma *Scancell*. The agreement gives the Danish company rights to develop the antibody in multiple novel potential therapeutic products for any and all potential disease areas, excluding cell therapy applications.

In exchange, Scancell gets an undisclosed upfront payment as well as $208m in potential development and commercial milestones for each product developed and commercialized, capped at $624m. Scancell also would be in line for sales royalties on any products brought to market.

The asset is a humanized antibody developed by Scancell using its novel anti-cancer GlyMab platform. It is one of five candidates currently in Scancell's antibody portfolio offering a reservoir of potential products for in-house clinical development or further deal-making, the biotech said.

Syncona Affiliate Will Buy AGTC For $73.5m

Gene therapy specialist *Applied Genetic Technologies Corporation* entered into a definitive agreement on 23 October for a newly established portfolio company of Syncona to acquire AGTC for a total consideration of $73.5m. Expected to close in Q4, the deal has been approved unanimously by AGTC's board.

Founded in 1999, AGTC is a public, clinical-stage biotech developing genetic therapies to treat ophthalmic, otologic and central nervous system (CNS) diseases. The firm currently is working to file its X-linked retinitis pigmentosa candidate AGTC-501 for approval at the US Food and Drug

Administration. (Also see "*AGTC Moves Past Biogen With Ophthalmic Gene Therapy*" - Scrip, 27 Jul, 2021.)

Syncona plans to acquire AGTC through a tender offer, for approximately $23.5m ($0.34 per share) at closing plus potential future payments of up to $50m (up to $0.73 per share) pursuant to contingent value rights (CVRs) tied to certain milestones related to transactions involving AGTC's assets and regulatory and commercial milestones related to AGTC's products. Syncona said it plans to fund the transaction with cash on hand.

Altamira Tightens Focus With Offloading Of Inner Ear R&D

Bermuda-based *Altamira Therapeutics Ltd.* (formerly *Auris Health, Inc.*) reported on 21 October that it will divest its inner ear therapeutics R&D portfolio to an undisclosed European buyer so that it can focus on its RNA delivery platforms and RNA therapeutics programs.

The buyer agreed to acquire 90% of the share capital of *Zilentin AG*, Altamira's Swiss subsidiary focused on partnering non-RNA programs in tinnitus and hearing loss, for $1m in cash. Formed in 2019, Zilentin has worked to develop novel, second-generation tinnitus treatments such as AM-102, in partnership with *King's College London*. The deal also confers a 30-day option for Zilentin's remaining legacy assets, including AM-101 (esketamine) for tinnitus, AM-111 (brimapitide) for hearing loss and AM-125 (intranasal betahistine) for vertigo for an upfront payment of $25m.

Beyond the 30 days, Zilentin will have a right of first refusal to acquire the assets through the end of 2022 with the option-exercise payment increasing by $1m per month. Altamira will be eligible to earn milestone payments of up to $55M should Zilentin opt in.

Apart from divesting its inner ear portfolio, Altamira is also trying to sell off another legacy asset, the 510(k)-cleared Bentrio (formerly AM-301) allergic rhinitis nasal spray, in the OTC consumer health sector.

Deals In Brief:

Exelixis, Inc. said on 3 November that it is paying *Catalent, Inc*. $30m up front for development rights to three antibodies derived from the latter's SMARTag bioconjugation platform for use in antibody-drug conjugates or other therapeutic modalities. Catalent also can realize development and sales milestones under the agreement, while follows Exelixis's announcement of two cancer-focused option deals on 2 November. (Also see "*Exelixis Looks To Early-Stage Option Rights As Low-Risk Pipeline Expansion Play*" - Scrip, 2 Nov, 2022.)

TFF Pharmaceuticals, Inc. and *Aptar Pharma* revealed on 3 November that they are combining their technology platforms in an effort to develop potential needle-free vaccines following the recommendations of the White House Summit on the Future of COVID-19 Vaccines this past July

of the need for alternative routes of administration. The two companies will pair TFF's Thin Film Freezing technology with Aptar's intranasal Unidose delivery system. TFF and Aptar said they are pursuing this approach to vaccination partly because direct immunization of the nasal mucosa could promote systemic and mucosal immunity.

Inventiva S.A. announced on 31 October that *AbbVie Inc.* has decided to end development of cedirogant (ABBV-157), a ROR gamma inverse agonist the latter inherited via a 2012 deal between Inventiva and then-*Abbott* subsidiary *Solvay SA*. The Phase II candidate – part of a larger collaboration in ROR gamma inverse agonist potential in autoimmune disease – is being shelved following the results of a non-clinical toxicology study, the firm said.

Adrestia Therapeutics signed a multi-target partnership on 25 October with Germany's *Proteros Biostructures GmbH* to accelerate discovery of first-in-class candidates for intractable neurologic and cardiomyopathic diseases. The agreement will enable UK-based Adrestia to accelerate its drug-discovery and -design activities with access to Proteros's protein biochemistry, assay development and high-throughput protein structure capabilities.

Genomic medicine-focused *NeuBase Therapeutics, Inc.* announced a research agreement on 21 October with an "undisclosed top 10 global health care company" to evaluate it PATrOL technology intended to address monogenetic diseases at their root causes. With its partner, NeuBase will evaluate candidates for three undisclosed indications, with the other company holding exclusive rights to license and development resulting candidates.

Switzerland's *Anokion SA* is getting financial and clinical development assistance from *Pfizer Inc.* for its celiac disease candidate KAN-101 under an 18 October agreement. Pfizer made a $35m equity investment through the Pfizer Breakthrough Growth Initiative, part of which Anokion said it will use to fund its Phase II clinical program of KAN-101, with dosing expected to begin during the second half of 2022. KAN-101 is designed to induce tolerance to gliadin, a core component of gluten, through natural pathways in the liver, the biotech said.

Tolmar Pharmaceuticals, Inc. was deemed the winning bidder on 14 October in a court-supervised asset auction of *Clarus Therapeutics Holdings, Inc.*'s portfolio, obtaining rights to the hypogonadism drug Jatenzo (testosterone undecanoate). (Also see "*Clarus Keeping Commercial Options Open For Oral Testosterone Jatenzo*" - Scrip, 28 Mar, 2019.) Tolmar agreed to pay $7.5m up front and contingent payments over a three-year period pegged to US product sales. Clarus will get a 6% royalty for US net sales up to $20m and 10% on sales greater than $20m, with a minimum annual payment of $500,000. It can further earn a 10% royalty if the product reaches annual sales thresholds of $30m, $50m or $70m. Clarus initiated Chapter 11 bankruptcy in October due to lack of funds for commercial operations. (Also see "*Finance Watch: With Limited Fundraising Options, Biotechs Restructure To Extend Cash Runways*" - Scrip, 19 Oct, 2022.)

Stay tuned for the next edition of Deal Watch. You can read more about other deals that have been covered in depth by Scrip and Generics Bulletin in recent days below:

(Also see "*With $120m, HI-Bio Aims To Rapidly Prove Approach To Immune-Mediated Diseases*" - Scrip, 2 Nov, 2022.)	Human Immunology Biosciences (HI-Bio) launched with $120m and two candidates from MorphoSys, including the CD38 inhibitor felzartamab already in the clinic for immune-mediated kidney diseases.
(Also see "*Exelixis Looks To Early-Stage Option Rights As Low-Risk Pipeline Expansion Play*" - Scrip, 2 Nov, 2022.)	The maker of Cabometyx wants to expand its oncology pipeline via deal-making but is wary of the high attrition rate in cancer. Option deals with Cybrexa and Sairopa may avoid some of that risk.
(Also see "*CSL Licenses Arcturus mRNA Technology, But COVID-19 Vaccine Remains Uncertain*" - Scrip, 2 Nov, 2022.)	The two companies signed a development and commercialization deal with a $200m upfront payment and milestones of up to $4.3bn.
(Also see "*Psychedelic Pioneers Team Up As Sector Consolidates*" - Scrip, 24 Oct, 2022.)	The psychedelics sector has been hit hard by lack of funding options of late but the prospects for Eleusis, which had to terminate a SPAC merger in the summer, look brighter with its acquisition by Beckley Psytech.
(Also see "*Sunshine Biopharma Swallows Up Nova Pharma In All-Canadian Deal*" - Generics Bulletin, 24 Oct, 2022.)	Sunshine Biopharma is set to bolster its portfolio by more than 50 products, while adding more than CAD10m to its top line, after snapping up its fellow Canadian firm Nova Pharma.
(Also see "*Gilead Invests In Synthetic Biology Partnership For Next Gen CAR-Ts*" - Scrip, 21 Oct, 2022.)	Gilead's Kite is the current leader in CAR-T, but is looking for ways to stay ahead of competitors and find safer and more effective next-generation therapies.
(Also see "*AbbVie Gains New Immunology Antibody Platform With DJS Buy*" - Scrip, 20 Oct, 2022.)	AbbVie will acquire privately-held UK antibody developer DJS with preclinical assets.
(Also see "*Roche Goes Big On KRAS-Mutated Cancers In Hookipa Pact*" - Scrip, 20 Oct, 2022.)	The Nobel Prize winner co-founded biotech can extend its cash runway into 2025, while Roche gains access to an immunotherapy with potential to treat a wide range of cancers.
(Also see "*Philogen Considers Partnering As Two*	The Swiss-Italian biotech firm's two lead

Lead Assets Near Market" - Scrip, 20 Oct, 2022.)	assets for cancer are expecting pivotal readouts next year, prompting it to consider partnering strategies and further substantiating its targeted R&D approach.
(Also see "*MPP Strikes Landmark Licensing Deal With Novartis On Nilotinib*" - Generics Bulletin, 20 Oct, 2022.)	The Medicines Patent Pool has struck a milestone voluntary licensing deal with new partner Novartis for nilotinib to treat chronic myeloid leukemia, representing the first MPP agreement in non-communicable diseases as well as the "first ever public health-oriented voluntary license agreement on a cancer medicine."
(Also see "*Zymeworks Deal Expands Jazz's Potential Oncology Presence*" - Scrip, 19 Oct, 2022.)	The deal focuses on the HER2-targeting bispecific antibody zanidatamab, in development for multiple solid tumor indications expressing HER2.
(Also see "*Advaxis To Seek New Life In Merger With Ayala*" - Scrip, 19 Oct, 2022.)	The new company will focus mainly on Ayala's lead candidate for desmoid tumors, but minority owner Advaxis will take over management.
(Also see "*Panaxia And Neuraxpharm Sign To Sell Medical Cannabis In The Czech Republic And Switzerland*" - Generics Bulletin, 18 Oct, 2022.)	Panaxia and Neuraxpharm have added the Czech Republic and Switzerland to their growing list of European markets for medical cannabis. Both countries have passed recent legislation to stimulate prescriptions of cannabis products.
(Also see "*Lilly Builds On Gene Therapy Focus With Akouos Takeout*" - Scrip, 18 Oct, 2022.)	With the planned $487m acquisition of sensorineural-focused Akouos, Lilly makes its second gene therapy M&A play in two years, on top of partnering/financing activity in the space.
(Also see "*Enliven Takes Precision Oncology Ambitions Public In Merger With Imara*" - Scrip, 14 Oct, 2022.)	The planned all-stock transaction will enable Enliven to take over Imara's Nasdaq listing with cash runway into 2026. Imara shareholders get contingent value rights tied to sold-off top candidate tovinontrine.