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Deal Watch: Novartis, Ionis Team Up Again In Cardiovascular Disease

by Joseph Haas

Plus deals involving ProQR/ Thea, Aeglea/Immedica, Ayala/Biolight, Quince/EryDel, ImmunoBiochem/ImmunoGen and GSK/LimmaTech, as well as deals in brief.

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

Novartis And Ionis Build On Earlier Akcea Alliance

Building on a collaboration begun in 2017 between *Novartis AG* and *Ionis Pharmaceuticals, Inc.* subsidiary *Akcea Therapeutics, Inc.*, the companies inked a collaboration and license agreement on 3 August for discovery, development and commercialization of a novel medicine for patients with Lp(a)-driven cardiovascular disease. Ionis gets a $60m upfront payment and can realize development, regulatory and commercial milestones as well as sales royalties.

Under the existing partnership, Novartis and Akcea are focused on development and commercialization of the antisense candidate pelacarsen, which Novartis is evaluating in a Phase III cardiovascular outcome study. (Also see "*Novartis Spreads Cardiovascular Bets with Ionis Antisense Option Deal*" - Scrip, 6 Jan, 2017.) The next-generation compound central to the new pact will be a potential follow-on to pelacarsen and will leverage Ionis's advancing RNA-targeting platform, the companies said.

ProQR To Get $13.8m Up Front From France's Théa

ProQR Therapeutics N.V. divested two late-stage ophthalmic assets – sepofarsen for Leber congenital amaurosis and ultevursen for Usher syndrome and retinitis pigmentosa – on 1 August to *Laboratoires Thea*. Under the agreement, ProQR will get €12.5m ($13.8m) up front and be eligible to earn €135m ($148.7m) in further development, regulatory and commercial milestones along with potential sales royalties.

Sepofarsen and ultevursen both had reached Phase III development before ProQR wound down development to shift resources to its Axiomer RNA-editing technology assets and the advancement of AX-0810 (cholestatic disease) and AX-1412 (cardiovascular disease) in August 2022. (Also see "*Finance Watch: The Job Cuts Keep Coming As Companies Try To Conserve Cash*" - Scrip, 16 Aug, 2022.)

ProQR utilizes next-generation RNA technology called Axiomer to develop therapeutics for various diseases. Axiomer uses a cell's own editing machinery called ADAR to make specific single nucleotide edits in RNA to reverse a mutation, according to the Belgian biotech.

Aeglea Sells Metabolic Disease Candidate To Immedica

Aeglea BioTherapeutics, Inc. agreed to sell the global rights to pegzilarginase, an investigational treatment for the rare metabolic disease arginase 1 deficiency (ARG1-D), on 27 July to *Immedica AB*. The Swedish firm will pay Aeglea $15m up front with the potential for up to $100m in regulatory and sales milestones.

The sale of pegzilarginase to Immedica supersedes the previous 2021 license agreement between the two companies, which has been terminated for the current asset-purchase agreement. They noted that the milestone payments are contingent on formal reimbursement decisions by national authorities in key European markets as well as pegzilarginase approval by the US Food and Drug Administration, among other events.

The upfront payment and contingent milestone payments if paid, will be distributed to holders of Aeglea's contingent value rights (CVR) pursuant to an agreement included in Aeglea's acquisition of Spyre Therapeutics in June. (Also see "*Aeglea Revives Fortunes By Joining Merck And Roivant In TL1A Drug Chase*" - Scrip, 23 Jun, 2023.)

Ayala Goes Public Via Merger With Israel's Biosight

Ayala Pharmaceuticals, Inc. and *BioSight Ltd.* agreed upon to a merger on 27 July under which the two companies will combine in an all-stock transaction. Upon completion, the combined company will operate under the name Ayala Pharmaceuticals and continue to trade on the OTCQX exchange under Ayala's current ticker symbol (ADXS). A portion of current Biosight shareholders have agreed to support the proposed transaction.

Founded in 2020, Biosight is a private clinical-stage biotech developing therapies for hematological malignancies and disorders. The Israeli firm's lead product, aspacytarabine (BST-236), is a proprietary anti-metabolite designed to address unmet medical needs by enabling high-dose chemotherapy with reduced systemic toxicity for acute myelogenous leukemia and myelodysplastic therapy.

Results from a recently completed Phase IIb study evaluating aspacytarabine as a single-agent,

first-line AML therapy demonstrated safety and single-agent activity. Additional studies are ongoing to evaluate the drug in combination with *AbbVie Inc.*'s Venclexta (venetoclax) as a first-line treatment for AML, as well as a second-line monotherapy for patients with relapsed or refractory MDS or AML.

The combined company will work to advance a portfolio of oncology assets, with a primary focus on Ayala's AL102, an oral gamma-secretase inhibitor (GSI), and Biosight's aspacytarabine. AL102 is currently being evaluated in the registrational RINGSIDE study in desmoid tumors. (Also see "*ESMO: Ayala In Shadow Of SpringWorks In Rare Cancer Race*" - Scrip, 13 Sep, 2022.) There are currently no FDA-approved therapies for the treatment of unresectable, recurrent or progressive desmoid tumors.

Under the agreement, upon completion of the merger, Biosight stockholders will own 55% of the combined company, with Ayala shareholders owning 45%. The merger agreement has been unanimously approved by each company's board, and is expected to close by the end of Q2 2023.

Quince To Acquire Rare Disease-Focused EryDel

Quince Therapeutics, Inc. agreed on 24 July to acquire privately held *EryDel SpA* in a stock-for-stock exchange with potential for downstream milestone payments to the latter firm's owners. Founded in 2007, Milan-headquartered EryDel deployed its autologous intracellular drug encapsulation (AIDE) technology to develop Phase III lead asset, EryDex, targeting a rare, fatal, pediatric neurological disease, ataxia-telangiectasia (A-T), which currently has no approved treatments. (Also see "*EryDex shows Phase II promise for rare disease ataxia telangiectasia*" - Scrip, 2 Mar, 2012.)

EryDex is an automated outpatient bedside technology to *ex-vivo* encapsulate dexamethasone sodium phosphate (DSP; a prodrug) into patients' red blood cells, which are then re-infused, allowing for the circulation of controlled, slow-release, low doses of dexamethasone (active drug) over the subsequent several weeks following treatment. EryDex has received orphan drug designation for the treatment of A-T both from the US FDA and the European Medicines Agency.

Upon completion of the transaction, EryDel stockholders will own approximately 16.7% of the combined company, with Quince shareholders owning the remainder. (subject to downward adjustment) or 7.25M shares. EryDel's shareholders also can realize $485m, including up to $5m in development milestones, $25m at US new drug application acceptance, $60m in approval milestones and $395m in market and sales milestones. No royalties will be due to EryDel stockholders under the agreement.

ImmunoBiochem Pairs Up With Immunogen On ADCs

Toronto's *ImmunoBiochem Corporation* signed a multi-target license and option agreement on 24 July with *ImmunoGen, Inc.* to advance novel, first-in-class antibody-drug conjugate (ADC)

therapeutics. The collaboration will combine ImmunoGen's proprietary linker and payload technologies with ImmunoBiochem's antibodies directed against specific targets.

Under the agreement, ImmunoGen will pay ImmunoBiochem an upfront fee in exchange for an exclusive license to existing antibodies directed against a specific undisclosed target. ImmunoBiochem also will be eligible to earn development, regulatory and commercial milestones and royalties under the agreement.

ImmunoGen will collaborate with ImmunoBiochem on preclinical activities, with the former assuming responsibility for the program's future clinical development and commercialization activities. ImmunoGen also obtains an option to select additional targets and antibodies to license based on certain preclinical work undertaken by ImmunoBiochem. If ImmunoGen exercises this option, ImmunoBiochem will get an option-exercise payment and ImmunoGen will assume responsibility for all subsequent R&D associated with that program.

GSK Licenses Shigellosis Vaccine To LimmaTech

Vaccine-focused *LimmaTech Biologics AG* in-licensed development and commercialization rights on 20 July to *GSK plc*'s quadrivalent bioconjugate vaccine candidate for shigellosis. In a circular transaction, GSK is offloading a pipeline asset it obtained when it acquired LimmaTech Bio's predecessor company, *GlycoVaxyn AG* , in 2015. (Also see "*GSK Acquires Conjugated Vaccine Expertise With GlycoVaxyn Purchase*" - Pink Sheet, 11 Feb, 2015.)

The vaccine candidate is composed of antigens from the four epidemiologically relevant *Shigella* bacterial strains and being tested in an ongoing Phase I/II dose-finding and age-descending (adults-children-infants) double-blind study to evaluate its safety and immunogenicity in nine-month-old infants. Data from the study are expected later this year.

LimmaTech Bio spun out from GlycoVaxyn after its acquisition by GSK and then signed a research collaboration with the pharma to develop novel bioconjugate antigen-based vaccines including a monovalent *Shigella* vaccine in cooperation with the Wellcome Trust. Following positive results from a proof-of-concept clinical trial with a monovalent Shigella vaccine, LimmaTech began development of a multivalent *Shigella* vaccine in 2018 with a *Wellcome Trust Sanger Institute* grant received by GSK for the new program.

In Brief:

- *Agios Pharmaceuticals, Inc.* announced on 3 August that it is paying $17.5m up front to license a preclinical small interfering RNA (siRNA) candidate to treat polycythemia vera from *Alnylam Pharmaceuticals Inc.* Agios said the candidate offers the opportunity for the first disease-modifying therapy in the rare hematological disorder. Under the deal, Alnylam can earn up to $130m in development and regulatory milestones, as well as sales royalties and commercial milestones.

- *Bayer AG* subsidiary *BlueRock Therapeutics LP* unveiled a collaboration and option agreement on 3 August with *bit.bio* for the discovery and manufacture of iPSC-derived regulatory T-cells (Tregs) for use in therapeutic applications. The agreement includes an option for Bluerock to license transcription factor (TF) combinations emerging from the collaboration as well as an option to license bit.bio's opti-ox precision cell programming technology to manufacture and develop iPSC-derived Tregs. UK-based bit.bio gets an undisclosed upfront payment with the potential for milestone payments and sales royalties.

- *MaxCyte, Inc.*, licensed non-exclusive clinical and commercial rights to use MaxCyte's Flow Electroporation technology and ExPERT platform on 1 August to *Prime Medicine, Inc.* In return, the cell-engineering specialist is entitled to annual license fees and program-related revenue.

- *Vyera Pharmaceuticals, LLC* and subsidiary Phoenixus AG entered into an asset purchase agreement with an unnamed buyer for Daraprim (pyrimethamine) and Vecamyl (mecamylamine hydrochloride) on 1 August in exchange for aggregate consideration of $650,000. Daraprim is indicated for the treatment of acute malaria and for chemoprophylaxis of malaria and treatment of toxoplasmosis infection when used conjointly with a sulfonamide. Vecamyl is an oral generic of mecamylamine hydrochloride for the management of moderately severe to severe essential hypertension and uncomplicated cases of malignant hypertension.

- GSK licensed *Soluble Therapeutics, Inc.* rights to its proprietary CyTaC (Cytotoxicity Targeting Chimera) platform and drug candidates on 1 August. In return, GSK obtained equity in Solu and can earn milestones and royalties on products derived from the platform. The technology unlocks antibody-intractable cell surface targets providing the capability to develop next-generation medicines that combine the qualities of biologics and small molecules, according to GSK. Concurrent with the deal, Solu raised $31m in seed financing.

- Celloram licensed global rights to develop CLM-022 as a treatment for liver disease to *Genfit SA* on 28 July. The total contract size is €160m ($176.2m), including milestones; additional financial details were not disclosed. CLM-022 is a synthetic pentacyclic triterpenoid derivative of a natural triterpenoid quinone methide, targeting NLRP3, under development by Celloram for the treatment of inflammatory bowel disease. Celloram said it plans to continue research with the candidate in various indications outside liver disease conditions.

- Under a binding term sheet, women's health-focused *Mithra Pharmaceuticals SA* licensed Montreal-based *Searchlight Pharma Inc.* exclusive rights on 31 July to market and sell menopause therapy Donesta (estetrol) in Canada. The Belgian firm can obtain up to €17.05m ($18.78m) in licensing fees and regulatory and sales-related milestones, plus net sales royalties under the agreement. In 2022, Mithra announced top-line efficacy results of the

Donesta Phase III clinical program, which demonstrated a reduction in vasomotor symptoms from baseline and compared to placebo, with all co-primary efficacy endpoints met with statistical significance. Depending on outcome of ongoing studies, Mithra intends to file the drug for US approval later this year and in Canada in 2024.

- *AstraZeneca PLC* now holds rights to transthyretin amyloidosis (ATTR) therapy eplontersen in Latin America under an expansion of a 2021 collaboration with Ionis announced on 28 July. (Also see "*AstraZeneca Boosts Rare Disease Pipeline With Ionis Antisense Candidate*" - Scrip, 7 Dec, 2021.) Latin America rights were held out of the original deal for the antisense drug candidate, with Ionis and the pharma to share US rights, while AstraZeneca held all other ex-US rights.

- *Roche Holding AG* will not exercise its option for HPV 16-positive solid tumors under a deal signed with *SQZ Biotechnologies Company* in 2018, the latter company revealed on 25 July. (Also see "*Deal Watch, Licensing & Alliances: Amgen Places $66m Bet On Genetic Sequencing*" - Scrip, 19 Oct, 2018.) Watertown, MA-based SQZ will regain full clinical development and commercialization rights for its programs targeting HPV 16-positive tumors and said intends to explore potential strategic partnerships to support the advancement of its oncology programs and platforms.

- Bermuda-based *Altamira Therapeutics Ltd.* licensed marketing and distribution rights on 20 July to Pharma Nordic for Bentrio, a nasal spray for protection against airborne allergens, in Norway and potentially other Scandinavian countries. The collaboration agreement will allow Norway-based Pharma Nordic to market and commercialize Bentrio in Norway beginning in the first quarter of 2024, and, subject to meeting certain milestones, also in Sweden, Finland and Denmark later.

- *Eikon Therapeutics, Inc.* acquired rights on 20 July to *Cleave Therapeutics, Inc.*'s preclinical assets, including a large chemical library spanning multiple targets in the AAA (ATPases Associated with diverse cellular Activities) family of ATPases. Concurrent with the Eikon deal, Cleave also noted that in an amendment to a 2021 collaboration, *CASI Pharmaceuticals, Inc.* has acquired the global rights to Cleave's oncology candidate CB-5339.

- Cardiovascular disease-focused Riparian Pharmaceuticals inked an exclusive license and research agreement on 19 July with *Pfizer Inc.* In exchange for rights to a Riparian preclinical program, Pfizer will make upfront and milestone payments, and pay royalties on sales of resulting therapeutics. Pfizer also will support Riparian’s efforts to discover further drug targets leading to vasoprotection and obtain an option on such targets. Riparian said its therapeutic programs target key vasoprotective pathways to reduce vascular inflammation and endothelial dysfunction.

- *Syros Pharmaceuticals, Inc.* revealed in an 18 July Securities and Exchange Commission filing that Pfizer has terminated a licensing deal the Cambridge, MA-based firm signed in 2019 with *Global Blood Therapeutics, Inc.* to discover and develop new sickle cell disease and beta thalassemia treatments. (Also see "*Deal Watch: Pfizer Licenses Skin-Targeted JAK Inhibitor Portfolio From Theravance*" - Scrip, 2 Jan, 2020.) The decision follows Pfizer's buyout of GBT for $5.4bn in August 2022. (Also see "*Pfizer's Buying Spree Continues With GBT, Gaining A Sickle Cell Disease Franchise*" - Scrip, 8 Aug, 2022.)

- AxoSim and *Vyant Bio, Inc.* announced a definitive agreement on 17 July under which the former will acquire the microBrain-associated assets of Vyant's *StemoniX Inc.* subsidiary. Vyant (previously known as *Cancer Genetics Italia Srl*) acquired StemoniX in 2021. (Also see "*Deal Watch: Jazz Breaks Into Immuno-Oncology Via Licensing Pact With Werewolf*" - Scrip, 7 Apr, 2022.) Under the transaction, AxoSim will pay Vyant $2.25m, of which $1.1m will be paid at close and the remainder based on milestones and financial considerations related to the deal's closing. In addition, AxoSim will assume approximately $1.2m of future lease-related liabilities.

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 "*TG Therapeutics Briumvi Deal Fails To Impress The Market*" - Scrip, 2 Aug, 2023.)	Linking up with Germany's Neuraxpharm to sell the multiple sclerosis drug Briumvi in Europe and elsewhere has gone down badly with investors but the bashing that TG Therapeutics' shares has taken seems excessive.
(Also see "*Revolution Picks Up Remains Of EQRx In All-Stock Deal*" - Scrip, 1 Aug, 2023.)	Revolution Medicines is looking to pump the $1bn it will get from the acquisition into its RAS inhibitor pipeline, with trials planned to start in 2024.
(Also see "*Ipsen's Desire For Dealmaking Burns Bright*" - Scrip, 31 Jul, 2023.)	Ipsen CEO David Loew tells *Scrip* that valuations to do deals with biotechs "are now at a reasonable level [and] we are screening companies very actively as we speak."
(Also see "*Roche CEO Outlines M&A Criteria*" - Scrip, 28 Jul, 2023.)	Every year, Roche looks at "more than 1,000 companies and 99.9% of the time, we say no," says CEO Thomas Schinecker, though he stressed that the Swiss group is open to deals of any size.
(Also see "*Biogen Buys Time For Leqembi*	By agreeing to pay $7.3bn for Reata and its

Ramp-Up With Reata Acquisition" - Scrip, 28 Jul, 2023.)	Friedrich's ataxia drug Skyclarys, "recalibrating" Biogen can be more patient with launch of Alzheimer's drug Leqembi.
(Also see "*Fast-Growing AstraZeneca Brushes Off China Rumors And Dato-DXd Concerns*" - Scrip, 28 Jul, 2023.)	AstraZeneca's Alexion buys portfolio of preclinical gene therapy programs from Pfizer. AstraZeneca exceeded revenue and profit expectations in Q2, but sought to calm concerns about a rumored China spin-out and underwhelming Phase III data.
(Also see "*AbbVie To Build On Relationship With Calibr Via Five-Year Extension*" - Scrip, 26 Jul, 2023.)	Previously partnered on CAR-T therapies for cancer and COVID-19 antivirals, AbbVie and Scripps' discovery unit Calibr unveil a five-year extension, including new targets and preclinical candidates.
(Also see "*Reading The FTC Tea Leaves: Investors Await Insights For M&A*" - Scrip, 26 Jul, 2023.)	Pfizer and Amgen both have large M&A deals under regulatory review, and investors will be eager to hear updates on how those transactions are progressing during Q2 reporting.
(Also see "*Galapagos Sees Global Market For Point-Of-Care CAR-T But Is Still On M&A Trail*" - Scrip, 25 Jul, 2023.)	Paul Stoffels is continuing his transformation of Galapagos into a company with CAR-T and small molecule platforms and is aiming to seal more M&A deals before the end of this year.
(Also see "*Infinity And MEI Re-evaluate Business Plans After Merger Falls Through*" - Scrip, 24 Jul, 2023.)	MEI shareholders declined to approve the all-stock merger with Infinity that would have combined the companies' cancer pipelines.
(Also see "*Eyebrows Raised As Roche Inks Cardiovascular Pact With Alnylam*" - Scrip, 24 Jul, 2023.)	Roche is so keen to get access to Alnylam's RNAi therapeutic targeting angiotensinogen that it is paying $310m upfront having only seen Phase I data.
(Also see "*Several Options Remain For Cidara's Flu Candidate After J&J Halts Development*" - Scrip, 21 Jul, 2023.)	Clinical work on Cidara's drug-Fc conjugate, CD388, has been stopped by partner Janssen amid a broader company shift, but there are several paths forward for Cidara after the asset showed early promise in a Phase IIa trial.
(Also see "*Sanofi Adds To Immunology Pipeline In Collaboration With Recludix*" - Scrip, 20 Jul, 2023.)	Sanofi gets global rights at the start of Phase II for the US biotech's preclinical program for inhibiting the STAT6 protein in respiratory

	and dermatologic disorders.
(Also see "*Pieris Looks For Way Out After AstraZeneca Exits Respiratory Collaboration*" - Scrip, 19 Jul, 2023.)	Pieris is hoping to either partner off its wholly owned pipeline or become a target for an acquisition or merger after AstraZeneca's asthma exit left it with dwindling cash, and a need to cut costs.