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Deal Watch: Merck KGaA Teams Up With Mersana On STING Agonist ADCs

by Joseph Haas

Mersana signs its third ADC partnership with big pharmas for the year with Merck agreement. Lilly expands its RNA editing partnership with ProQR, which now has the potential to earn an additional $2.5bn. Novartis continues its divestment efforts in deals with Harrow, Erasca.

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

Mersana Ends 2022 With Third Big Pharma ADC Deal, This Time With Merck

Mersana Therapeutics, Inc. and *Merck KGaA* have agreed to develop and commercialize novel antibody-drug conjugates (ADC) based on the former's Immunosynthen STING-agonist ADC platform, marking the US biotech's third ADC-oriented partnership with big pharma in 2022.

Under the terms of the deal, Mersana will use Immunosynthen to develop ADC candidates against up to two targets to conjugate with proprietary antibodies from Merck. The Cambridge, MA based-firm will receive $30m upfront and is eligible for up to $800m in milestones as well as low double-digit royalties on net sales.

Immunosynthen is designed to generate novel ADCs that can trigger localized STING signaling in both tumor-resident immune cells and antigen-expressing tumor cells. This "one-two punch" approach has the potential to enhance anti-tumor activity when compared with other approaches that activate only the immune cells.

Preclinical Immunosynthen data across multiple targets and tumor models have attained complete regression of tumors *in vivo* after a single dose. Leerink Swann analyst Jonathan Chang said in a 23 December note the deal was a positive source of non-dilutive capital for Mersana and further validated its platform.

This is certainly not the first partnership Mersana has forged involving Immunosynthen this year. In August, the firm clinched an option agreement with *GSK plc* for its then-preclinical HER2-targeting ADC, XMT-2056, which was also developed using the platform.

Under the terms of that deal, Mersana received $100m upfront and is eligible for up to $1.36bn in option payments and various milestones as well tiered double-digit royalties on net sales. XMT-2056 is currently recruiting for a Phase I dose escalation and expansion trial in previously treated patients with advanced or recurring solid tumors expressing HER2 according to the US ClinicalTrials.gov database.

The firm's other technology platforms have also garnered significant attention. At the start of the year, Mersana received $40m upfront from *Johnson & Johnson* under a research and license agreement to develop ADCs for three targets based on its proprietary Dolasynthen platform, with utilizes Mersana's clinically validated DolaLock microtubule inhibitor payload.

Lilly Adds Nervous System Targets To ProQR Alliance

Eli Lilly and Company and *ProQR Therapeutics N.V.* have expanded their September 2021 collaboration and licensing agreement to apply the latter's Axiomer RNA-editing platform for development of novel therapies for genetic liver and nervous disorders. The work to date has resulted in "significantly increased editing efficiency and refined biodistribution in both the liver and nervous system, opening up new potential applications to not only correct known mutations, but also introduce protective variants in specific transcripts," leading to the 22 December announcement that Lilly was doubling down on the Axiomer platform.

The Dutch biotech will get $75m up front under the deal revision along with an equity investment from Lilly in exchange for applying the Axiomer platform to additional targets in the central nervous and peripheral nervous systems. Lilly also gets an option to further expand the partnership for a consideration of $50m. In addition, Lilly can elect to provide ProQR with access to the company's proprietary delivery technology for its wholly owned pipeline.

Based on the original agreement and terms of the expansion, ProQR could realize up to $3.75bn in research, development and commercialization milestones (including an additional $2.5bn in milestones for the expansion), plus royalties. (Also see "*Lilly To Try ProQR's RNA-Editing Technology In Liver, Neurology Indications*" - Scrip, 9 Sep, 2021.)

Harrow Obtains Five Ophthalmic Drugs From Novartis

Nashville-based *Harrow Health, Inc.* licensed exclusive US commercial rights on 14 December to five FDA-approved ophthalmic products from *Novartis AG*.

The deal confers rights to the following ophthalmic products: Ilevro (nepafenac ophthalmic suspension) for pain and inflammation associated with cataract surgery; Nevanac (nepafenac

ophthalmic suspension), also an eye drop for pain and inflammation associated with cataract surgery; Vigamox (moxifloxacin hydrochloride ophthalmic solution) for the treatment of bacterial conjunctivitis; Maxidex (dexamethasone ophthalmic suspension) 0.1%, a steroid eye drop for steroid-responsive inflammatory conditions; and Triesence (triamcinolone acetonide injectable suspension) 40 mg/ml, a steroid injection for certain ophthalmic diseases and for visualization during vitrectomy.

Under the agreement, Harrow will pay Novartis $130m at closing, with a potential $45m milestone due upon commercial availability of Triesence, expected in the second half of 2023.

Erasca Licenses Phase III-Ready RAF Inhibitor From Novartis

Erasca, Inc. inked a global license agreement on 9 December with Novartis for naporafenib, a Phase II, pivotal-ready pan-RAF inhibitor with a potential first-in-class and best-in-class profile in NRAS mutant melanoma and other RAS/MAPK pathway-driven tumors.

Under the agreement, Erasca will pay to Novartis $20m up front and issue $80m in shares of its common stock priced at $6.50 per share (a 10% discount). Novartis could also realize up to $80m in regulatory milestones and up to $200m in sales milestones, along with single-digit royalties on net sales of naporafenib.

In tandem with the deal, Erasca grossed $100m on 9 December by selling 15.38 million shares of stock at $6.50 each. (Also see "*Finance Watch: Public Biopharma Firms Take Advantage Of Relative Upswing*" - Scrip, 19 Dec, 2022.) The company said it will use the proceeds plus its existing cash to advance its preclinical and clinical assets, some of which also are being studied under a five-year collaboration with *University of Texas MD Anderson Cancer Center*.

To date, naporafenib has been dosed in over 500 patients across multiple trials and has demonstrated preliminary clinical proof-of-concept as well as favorable safety and tolerability data both as a single agent and in combination with other molecularly targeted and immuno-oncology therapies.

VistaGen Acquires Pherin, Phase III SAD Candidate

VistaGen Therapeutics, Inc. and *Pherin Pharmaceuticals, Inc.* announced a definitive agreement on 21 December for VistaGen to acquire Pherin for approximately 12.4 million shares of its common stock and a small amount of cash. VistaGen holds license rights to Pherin's lead candidate, PH94B, under a 2018 agreement; in July, the drug failed to meet the primary endpoint in the first of two Phase III trials for social anxiety disorder. (Also see "*VistaGen Staggered By Latest Clinical Setback, This Time In Social Anxiety*" - Scrip, 22 Jul, 2022.)

Upon closing, VistaGen will acquire Pherin's entire pherine pipeline, which also includes Phase II development of PH94B for adjustment disorder with anxiety, and PH10, in clinical development

for major depressive disorder. Also in the pipeline are early-stage clinical candidates for cognition improvement, migraine and hot flashes, and appetite-related disorders.

Founded in 1991, Pherin has focused on discovering and developing pherines for acute, intermittent and long-term treatment for a range of human diseases and disorders. Pherines are odorless and tasteless investigational neuroactive steroids that engage receptors and neurons in nasal passages.

Ordaōs And Yatiri Team Up In Acute Myeloid Leukemia

Ordaos Bio and *Yatiri Bio* signed a joint development agreement on 19 December to create new therapeutics for two novel targets in acute myeloid leukemia (AML). No financial terms were disclosed.

Ordaōs employs its machine-driven Design Engine technology to create miniPRO proteins, which can offer the power and performance of antibodies but are more configurable, stable and easier to manufacture, according to the company. Yatiri will use its proteomics platform to integrate diverse patient and proteome data streams for use in *ex vivo* model systems to develop personalized medicines.

Specifically, Yatiri will use its proteomics technology to match AML patient samples with model systems to identify two cell surface therapeutic targets for high-risk AML. Ordaōs then will create *in silico* novel protein candidates and perform *in vitro* validation of those leads. Once the targets are validated, Ordaōs and Yatiri said they will jointly develop candidates for an investigation new drug (IND) submission.

GRI Bio Goes Public Via Merger With Vallon

Vallon Pharmaceuticals Inc. and *GRI Bio, Inc.* agreed to merge on 13 December in all-stock transaction that will enable GRI Bio to go public. The transaction is expected to close in the first quarter of 2023.

Founded in 2009, GRI Bio is a clinical-stage biotech focused on changing the way inflammatory disease is treated by targeting natural killer immune T-cells (NKT) earlier in the inflammatory chain than the current standard of care, to interrupt disease progression. GRI Bio's lead program, GRI-0621 is a small molecule RAR-βɣ dual agonist that has been shown to inhibit NKT I cells in patients and improve fibrosis in multiple disease models. GRI Bio is planning to launch a Phase IIa biomarker study evaluating GRI-0621 for the treatment in idiopathic pulmonary fibrosis with data expected in Q2 2024.

Concurrent with execution of the merger, Altium Capital will invest approximately $15m in GRI with a commitment for an additional $10m future investment. in the combined company. Equity

holders of GRI Bio are expected to own approximately 83% of the combined company on a fully diluted basis, with Vallon shareholders owning the rest.

In Brief:

- Singapore's Hyphens Pharma International Ltd. announced on 23 December that it has licensed commercial rights to the topical acne medication Winlevi (clascoterone) from a subsidiary of *Cosmo Pharmaceuticals N.V.* The rights cover 10 nations in Southeast Asia.

- Germany's *Ethris GmbH* began a collaboration on 21 December with UK-based *DIOSynVax* to jointly develop a protective mRNA vaccine candidate against a broad range of Betacoronaviruses utilizing the company's mRNA modification and design technologies as well as its lipidoid nanoparticle and stabilization platforms. The collaboration will use a $42m grant to DIOSynVax by the Coalition for Epidemic Preparedness Innovations (CEPI) to support development through a Phase I/II clinical trial.

- *AbCellera Biologics Inc.* entered a multi-year, multi-target strategic collaboration on 15 December with *AbbVie Inc.* that will leverage the former's antibody discovery and development engine to deliver optimized development candidates for up to five targets selected by AbbVie across multiple indications. AbCellera will get research funding and could earn clinical and commercial milestones and sales royalties under the deal.

- *Praxis Precision Medicines, Inc.* and *UCB S.A.* signed a collaboration on 13 December, based upon Praxis' PRAX-020 program, for the discovery of small molecule therapeutics as potential treatments of KCNT1 related epilepsies. Under the collaboration, UCB gets an option to global development and commercialization rights to any resulting KCNT1 candidate. Praxis will receive an undisclosed upfront payment and could realize up $100m under the agreement, plus potential sales royalties.

- *Tonix Pharmaceuticals Holding Corp.* licensed three monoclonal antibodies for the treatment or prevention of COVID-19 on 12 December from *Curia Global*, (formerly *Albany Molecular Research, Inc.*) Tonix said it believes the licensed murine mAbs represent a new approach to treating SARS-CoV-2 infection.

- *Tris Pharma, Inc.*said on 7 December that it acquired rights from an undisclosed partner to TRN-261, a non-opioid drug candidate that could address multiple acute and chronic pain indications. The company said the drug has been submitted for a non-pain indication but received a complete response letter from the US Food and Drug Administration, which was not related to safety concerns about the candidate. Several studies of TRN-261 established proof of concept within both acute and chronic pain conditions for which only opioid-based treatment options are available, the company noted.

- The UK's *Essential Pharma* acquired global rights to the antipsychotic drugs Haldol (haloperidol) and Haldol Decanoate (haloperidol decanoate) on 7 December from *Janssen Pharmaceutica NV*. The products are currently marketed in the US as well as in more than 60 countries across EMEA, Latin America and the Asia-Pacific regions. No financial terms were disclosed.

- *Caris Life Sciences* and *Hummingbird Bioscience* unveiled a collaboration on 6 December to advance clinical development of the latter's anti-HER3 antibody, HMBD-001, for solid tumors. The candidate uniquely targets an epitope on the critical dimerization interface of tumors, the partners said. They plan to evaluate biomarkers to study the clinical utility of HMBD-001 as well as to drive patient recruitment and clinical trial access.

- AbbVie and *HotSpot Therapeutics, Inc.* inked a global collaboration and option agreement on 6 December for the latter's discovery-stage IRF5 program for the treatment of autoimmune diseases. HotSpot gets an upfront payment of $40m and could earn up to $295 in option fees and research and development milestones, with potential for further commercial milestones as well as tiered sales royalties.

- *Pfizer Inc.* and *Clear Creek Bio, Inc.* announced a collaboration and license agreement on 6 December to advance the discovery and development of potential inhibitors of the SARS-CoV-2 papain-like protease for the oral treatment of COVID-19. Clear Creek will receive an undisclosed upfront payment and be eligible for additional potential milestone payments plus royalties on future product sales.

- *Evaxion Biotech A/S* signed a vaccine discovery collaboration agreement on 6 December with fellow Danish biotech *ExpreS2ion Biotech Holding AB* for joint development of a novel cytomegalovirus vaccine. During the discovery phase, Evaxion will use its RAVEN artificial intelligence platform to design a vaccine that can elicit both cellular and humoral/antibody responses. Under the agreement, ExpreS2ion holds the right to license the candidate, with the companies dividing research and intellectual property licensing costs equally until 2025.

- UK-based *Immunocore, Ltd.* and *Gadeta B.V.* unveiled a collaboration on 2 December for the first γδ ImmTAC for solid tumors, including colorectal cancer. Netherlands-based Gadeta can realize upfront, near-term option fee and research milestone payments under the deal. If Immunocore exercises its option, Gadeta also could earn development and commercial milestones as well as sales royalties.

- AbCellera and *Rallybio Corp.* announced a multi-year, multi-target alliance on 1 December to discover, develop and commercialize novel antibody-based therapeutics for rare diseases. Under the agreement, the firms will co-develop up to five rare disease therapeutic targets, which will be chosen together by both companies. The partnership's first program will focus

on addressing unmet needs of patients with rare metabolic diseases.

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 "*LegoChem's $1.2bn ADC Platform Deal With Amgen Signals Continued Big Pharma Interest*" - Scrip, 23 Dec, 2022.)	LegoChem's hefty out-licensing deal with Amgen seems to further prove global pharma's keen interest in the Korean ADC leader's technology, said to be differentiated with safer margins.
(Also see "*Gilead's Kite To Buy Tmunity, Enhancing CAR-T Pipeline And Manufacturing*" - Scrip, 20 Dec, 2022.)	Kite CEO Christie Shaw said Tmunity brings three advantages: armored CAR-Ts, manufacturing technology and an ongoing research deal with the University of Pennsylvania.
(Also see "*Sanofi Gains New Innate Program In Expanded Collaboration*" - Scrip, 19 Dec, 2022.)	Innate will receive €25m up front from Sanofi for an exclusive license to a new natural killer (NK) cell engager program and options to two additional targets.
(Also see "*Sosei Heptares Adds Lilly To Big Pharma Client List*" - Scrip, 16 Dec, 2022.)	Sosei is ending the year on a high, banking $37m upfront from a pact with Eli Lilly that will focus on finding small molecules which modulate G protein-coupled receptor (GPCR) targets.
(Also see "*Midatech Bets on Bioasis Merger For Survival*" - Scrip, 15 Dec, 2022.)	With just enough cash to stay afloat until the first quarter, Midatech is linking up with US-based, Canada-listed Bioasis to create a new rare disease player, Biodexa.
(Also see "*Wave Banks $170m Upfront In GSK Oligonucleotide Deal, Analysts Back Shift To Partnership Model*" - Scrip, 14 Dec, 2022.)	Wave Life Sciences has out-licensed a preclinical candidate to GSK as the firms pair up to discover and develop multiple oligonucleotide assets.
(Also see "*Takeda Aims At BMS's Sotyktu In $4bn Deal For Nimbus's TYK2 Inhibitor*" - Scrip, 13 Dec, 2022.)	Takeda's R&D chief Andy Plump said his company has seen data indicating game-changing characteristics for TAK-279 in psoriasis. It plans to bring the candidate into Phase III next year.
(Also see "*Alvotech Targets MENA In Multi-Biosimilar Commercialization Deal*" - Generics Bulletin, 12 Dec, 2022.)	Three firms across Europe and North Africa sign to sell Alvotech biosimilar candidates in 19 MENA countries as the Icelandic developer

	shifts focus from R&D to global commercialization.
(Also see "*Amgen To Enhance Rare Disease Franchise With $27.8bn Horizon Takeover*" - Scrip, 12 Dec, 2022.)	Amgen has announced its biggest acquisition to date in the form of a takeover of Horizon that should expand its rare disease franchise and stave off concerns about internal products facing biosimilar competition.
(Also see "*Nordic Nanovector In Limbo As Merger Collapses*" - Scrip, 12 Dec, 2022.)	The board has resigned at the crisis-hit Norwegian firm after shareholders voted against a reverse merger with APIM Therapeutics.
(Also see "*Deal With Arcellx Gives Gilead New Beachhead In Multiple Myeloma*" - Scrip, 9 Dec, 2022.)	Months after terminating its Phase I BCMA-targeting CAR-T program and on the eve of ASH, Gilead's Kite announced a deal with Arcellx for a CAR-T that has already shown promising data.
(Also see "*Vertex Adds To Myotonic Dystrophy Effort With Entrada Collaboration*" - Scrip, 8 Dec, 2022.)	Entrada gets $250m cash and equity up front under four-year deal, which extends its runway and will enable it to focus on Duchenne muscular dystrophy. Vertex further diversifies its pipeline with a novel drug class.
(Also see "*MorphoSys Teams Up Again With Novartis For Preclinical Cancer Program*" - Scrip, 7 Dec, 2022.)	MorphoSys announced in March that it was terminating the early-stage oncology R&D projects that came with its purchase of Constellation last year and Novartis has snapped up one of them.
(Also see "*Horizon Megadeal: J&J Out, Experts Say Sanofi Could Have Edge On Amgen*" - Scrip, 6 Dec, 2022.)	Janssen has dropped out of the running to acquire Irish biotech Horizon, leaving Sanofi and Amgen to vie over the potential megadeal, with some observers identifying the former as the better fit.
(Also see "*TherapeuticsMD Finds New Exit With Mayne Pharma Licensing Pact*" - Scrip, 5 Dec, 2022.)	After failure to close of a potential $177m buyout by EW Pharma, TherapeuticsMD will resolve its debt by selling its three-product women's health portfolio to Mayne.
(Also see "*Biocon And Zentiva Sign Liraglutide Deal For 30 European Countries*" - Generics Bulletin, 2 Dec, 2022.)	Zentiva gains semi-exclusive commercialization rights to Biocon's liraglutide drug-device combination in 30 countries, following a string of similar deals for the company since its 2018 acquisition.

(Also see "*Lupin Turns Up Heat With Bausch Brands Acquisition, Perforomist Generic Launch*" - Generics Bulletin, 1 Dec, 2022.)	Two acquisitions of brands in as many months, Lupin has stepped up its game in the Americas. A buyout of nine established Bausch Health brands follows rights to two from Sunovion. While it awaits news on generic(g) Spiriva, the launch of gPerforomist will help expand Lupin's respiratory franchise.
(Also see "*Pfizer Returns To Roivant As Development Partner For A Second Time*" - Scrip, 1 Dec, 2022.)	Roivant will form a new "vant" company to develop and commercialize Pfizer's TL1A inhibitor for ulcerative colitis.
(Also see "*BioNTech Bolsters Cancer Immunotherapy Ambitions In Pact With Cash-Poor Ryvu*" - Scrip, 30 Nov, 2022.)	German firm gets license rights to Ryvu's STING agonist portfolio in addition to collaborating on immunomodulators. Ryvu adds need cash via upfront and equity payments from BioNTech.

Editor's Note: This article was updated on 03/01/2022 to clarify that Mersana has a deal with Merck KGaA.