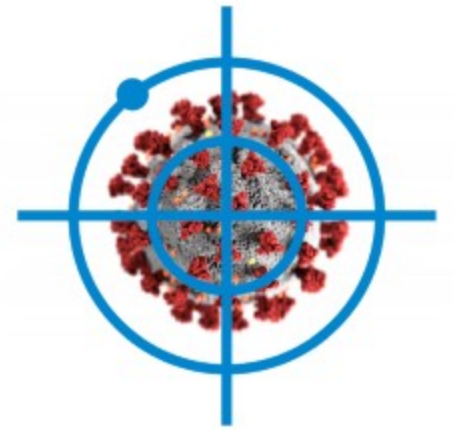
Antibody News You Should Know

January 1 - 15, 2021

Attention Antibodies to Watch fans,
"Antibodies to Watch in 2021" can be downloaded from the Society's publications page!



COVID-19 intervention news

On January 8, 2021, the clinicaltrials.gov record for the Phase 1 study (NCT04454398) of Sorrento's anti-SARS-CoV-2 antibody STI-1499 (COVI-GUARD) in hospitalized patients with moderate COVID-19 was updated to indicate that the study has been **withdrawn due to difficulty recruiting**.

On January 12, 2021, Vir Biotechnology, Inc. and GlaxoSmithKline plc announced an agreement with the U.K.-based AGILE initiative to **evaluate VIR-7832 in patients with mild to moderate COVID-19 in a Phase 1b/2a clinical trial**. The start of the study is anticipated in Q1 2021.

- VIR-7832 is an anti-SARS-CoV-2 antibody with an enhanced ability to clear infected cells and the potential to enhance virus-specific T cell function.

Updates on non-COVID-19 interventions

Company acquisitions completed or pending

On January 4, 2021, **Charles River Laboratories International, Inc. announced that it acquired of Distributed Bio, Inc.** on December 31, 2020. The companies had an exclusive partnership that was initiated in October 2018. The transaction combines Distributed Bio's antibody libraries and immuno-engineering platform with Charles River's extensive drug discovery and non-clinical development expertise to create an integrated, end-to-end platform for therapeutic antibody and cell and gene therapy discovery and development.

On January 11, 2021, Sanofi and Kymab announced that they had entered into an agreement under which **Sanofi will acquire Kymab** for an upfront payment of approximately $1.1 billion and up to $350 million upon achievement of certain milestones. The transaction will result in Sanofi having full global rights to KY1005 and KY1044.

- KY1005 is an anti-OX40 ligand human monoclonal antibody evaluated in a Phase 2 study of patients with atopic dermatitis.
- KY1044 is an ICOS agonist monoclonal antibody in early Phase 1/2 development for advanced cancers.

FDA designations granted

On January 5, 2021, Roche announced that **tiragolumab has been granted**

Breakthrough Therapy Designation by the US Food and Drug Administration (FDA), in combination with Tecentriq® (atezolizumab) for the first-line treatment of people with metastatic non-small cell lung cancer whose tumors have high PD-L1 expression with no EGFR or ALK genomic tumor aberrations. The combination of tiragolumab and atezolizumab is being evaluated in two Phase 3 studies of patients with NSCLC.

- Tiragolumab is an anti-TIGIT human monoclonal antibody derived from Ligand Pharmaceutical's OmniAb® technology platform.

On January 07, 2021, Merus N.V. announced that the FDA granted **Fast Track Designation to zenocutuzumab** for the treatment of patients with metastatic solid tumors harboring NRG1 gene fusions that have progressed on standard of care therapy. Zenocutuzumab is undergoing evaluation in a Phase 1/2 study for this indication.

- Zenocutuzumab is a full-length IgG1 bispecific antibody that simultaneously targets the growth factor receptors HER2 and HER3.

Initiation of first Phase 1 studies

On January 5, 2021, details were posted on clincaltrials.gov for a first in human dose escalation and expansion study (**NCT04695847**) of M1231 as a single agent in participants with advanced solid tumors. Sponsored by EMD Serono Research & Development Institute, Inc., this study has an estimated enrollment of 84 patients and an estimated start date in January 2021.

- M1231 is an anti-MUC1-EGFR bispecific antibody-drug conjugate (ADC) derived from the strand-exchange engineered domain (SEED) platform from Merck KGaA.

On January 13, 2021, details were posted on clincaltrials.gov for a Phase 1a/1b study (**NCT04708210**) to evaluate the safety, tolerance and preliminary efficacy of IBI319 in patients with advanced malignant tumors. Sponsored by Innovent

Biologics (Suzhou) Co. Ltd., this study has an estimated enrollment of 256 patients and an estimated start date in February 2021.

- IBI319 is a bispecific antibody that incorporates the sintilimab anti-PD-1 binding backbone; the second target has not been disclosed.

On January 13, 2021, Jounce Therapeutics, Inc. announced the initiation of patient enrollment in the INNATE **Phase 1 clinical study of its lead macrophage program JTX-8064** as a monotherapy and in combination with either JTX-4014, its internal PD-1 inhibitor, or pembrolizumab in patients with advanced solid tumors.

- JTX-8064 is a humanized IgG4 monoclonal antibody designed to specifically bind to the macrophage receptor Leukocyte Immunoglobulin Like Receptor B2 (LILRB2/ILT4).

Initiation of first Phase 3 studies

On January 4, 2021, Genmab A/S announced the initiation of the innovaTV 301 trial (NCT04697628), a global **Phase 3 study to evaluate the efficacy of tisotumab vedotin** compared to chemotherapy in patients with recurrent or metastatic cervical cancer who have received one or two prior lines of systemic therapy. In the innovaTV 301 trial, tisotumab vedotin will be compared with physician's choice single agent chemotherapy.

- Tisotumab vedotin is an ADC composed of Genmab's human IgG1 monoclonal antibody specific for tissue factor and Seagen's ADC technology that utilizes a protease-cleavable linker that covalently attaches the microtubule-disrupting agent monomethyl auristatin E to the antibody and releases it upon internalization.

On January 8, 2021, details were posted on clincaltrials.gov for is a randomized, double-blind, placebo-controlled, parallel group Phase 3 Study (**NCT04701983**) to evaluate the efficacy, safety, and tolerability of

SAR440340/REGN3500/Itepekimab in patients with moderate-to-severe chronic obstructive pulmonary disease. This study is recruiting a total of ~ 930 patients.

- Itepekimab is an anti-IL-33 IgG4 monoclonal antibody developed by Sanofi and Regeneron.

On January 14, 2021, details were posted on clincaltrials.gov for a Phase 3 randomized, double-blind, placebo-controlled study (**NCT04709575**) assessing the efficacy of a mixture of anti-Bet v 1 monoclonal antibodies to reduce symptoms of seasonal allergic rhinitis. Sponsored by Regeneron, this study has an estimated enrollment of 300 patients and an estimated start date in January 2021.

- REGN5713-5714-5715 are human monoclonal antibodies that bind birch pollen allergen Bet v 1.

FDA action date for teplizumab's BLA

On January 4, 2021, Provention Bio, Inc. announced that the Biologics License Application for teplizumab for the delay or prevention of clinical type 1 diabetes in at-risk individuals has been filed by the FDA, granted a Priority Review and assigned a **user fee goal date of July 2, 2021**. FDA is planning to hold an advisory committee meeting, tentatively scheduled for May 27, 2021.

- Teplizumab is humanized, non-Fc receptor binding, anti-CD3 monoclonal antibody.

Attending a virtual meeting soon?

Antibody News You Should Know

January 15 - 31, 2021

COVID-19 intervention news

On January 15, 2021, **Jemincare Group announced that it has initiated the Phase 1 clinical trial of an anti-SARS-CoV-2 neutralizing antibody (JMB2002)** produced from a high yield stable cell line. JMB2002 is derived from a naive human B cell antibody library from healthy donors. Preclinical studies indicated that JMB2002 could effectively neutralize live virus infection of Vero E6 cells, and the antibody showed potent binding and blocking activities to the spike glycoproteins of mutant viruses.

On January 25, 2021, **Elasmogen Ltd announced a panel of novel, potent, anti-Covid-19 therapeutic candidates** identified through collaboration with U.S. research partners. The newly identified anti-Covid-19 Spike protein VNARs block infection of the virus (in live viral assays) at doses as low as 200 pM, equivalent to the best reported antibodies and much better than many. This new approach has been achieved through a close partnership with the University of Minnesota, USA. Initial funding for this work was received from the Chief Scientist Group, Scottish Government and was co-ordinated through the University of Aberdeen.

- VNARs, derived from the variable region of shark IgG novel antigen receptors, are the smallest naturally occurring binding domains in the vertebrate kingdom.

On January 27, 2021, Eli Lilly and Company, Vir Biotechnology, Inc. and GlaxoSmithKline plc announced a collaboration to evaluate a combination of two COVID-19 therapies in low-risk patients with mild to moderate COVID-19. Lilly has expanded its ongoing BLAZE-4 trial (NCT04634409) to evaluate the administration of **bamlanivimab (LY-CoV555) 700mg with VIR-7831/GSK4182136 500mg**. Bamlanivimab alone has been granted Emergency Use Authorization by the U.S. Food and Drug Administration (FDA), VIR-7831 is an investigational compound, not approved by the FDA or any other regulatory authority.

- Bamlanivimab and VIR-7831/GSK4182136 are anti-SARS-CoV-2 antibodies that bind to different epitopes of the viral spike protein.

Updates on non-COVID-19 interventions

INDs allowed by FDA

On January 26, 2021, Teneobio, Inc. and its affiliate TeneoThree, Inc. announced that their investigational new drug application (**IND) for TNB-585**, a bispecific T-cell engaging antibody for the treatment of metastatic castrate resistant prostate cancer was cleared for the initiation of Phase 1 clinical studies by the FDA on January 23, 2021.

- TNB-585 targets prostate-specific membrane antigen on tumor cells and CD3 on T cells.

On January 27, 2021, Samsung Biologics announced FDA had cleared the **IND for EU101(NOV1801)**. In 2018, Korea's National OncoVenture, a government-funded virtual oncology drug development program, approached Samsung Biologics for the development of EU101(NOV1801), an therapeutic monoclonal antibody provided by Eutilex.

- EU101(NOV1801) targets 4-1BB, (CD137, TNFRSF9), an inducible costimulatory receptor expressed on activated T cells.

Antibodies entering first-in-human studies

On January 26, 2021, details were posted on clincaltrials.gov for a Phase 1, first-in-human clinical study (**NCT04725474**) of CTL-002 given as monotherapy and/or in combination with an anti-PD-1 checkpoint inhibitor in patients with advanced-stage, relapsed/refractory solid tumors. Patients are eligible for the study if they relapsed post or were refractory to a prior anti-PD-1/PD-L1 therapy and have exhausted all available approved standard treatments or are not eligible for them anymore.

- CTL-002 is a monoclonal antibody that targets growth differentiation factor 15.

On January 28, 2021, Evotec SE announced that **EVT894 (formerly SAR440894)**, a monoclonal antibody to treat and potentially prevent chikungunya virus infections, has entered clinical development. The Phase 1, randomized, double-blind, single center, single dose escalation study (NCT04441905) to evaluate the safety, pharmacokinetics, and immunogenicity of EVT894 vs placebo in healthy volunteers is sponsored and funded by the National Institute of Allergy and Infectious Diseases.

- EVT894 is a human antibody that targets Chikungunya virus.

Phase 3 studies started

On January 22, 2021, details were posted on clinicaltrials.gov for 3 Phase 3

studies of GSK3511294 in asthma. NCT04719832 and NCT04718103 are 52-week, randomized, double-blind, placebo-controlled, parallel-group, multi-center studies of the efficacy and safety of GSK3511294 adjunctive therapy in adult and adolescent participants with severe uncontrolled asthma with an eosinophilic phenotype. NCT04718389 is a 52-week, randomized, double-blind, double-dummy, parallel group, multi-centre, non-inferiority study assessing exacerbation rate, additional measures of asthma control and safety in adult and adolescent severe asthmatic participants with an eosinophilic phenotype treated with GSK3511294 compared with mepolizumab or benralizumab. All three studies are scheduled to start in late January 2021.

- GSK3511294 is a humanized monoclonal antibody antagonist of Interleukin-5.

On January 22, 2021, details were posted on clinicaltrials.gov for a Phase 3, randomized, double-blind, adaptive, placebo/paclitaxel-controlled study (**NCT04729608**) of AVB-S6-500 in combination with paclitaxel in patients with platinum-resistant recurrent ovarian cancer. The study has an estimated enrollment of 500 patients and an estimated start date in February 2021.

- AVB-S6-500 is an is a fusion of the extracellular domain of AXL (the receptor for GAS6) with a human IgG1 Fc domain.

Updates on BLAs

On January 19, 2021, Omeros Corporation announced that the Biologics License Application (BLA) for narsoplimab for the treatment of hematopoietic stem cell transplant-associated thrombotic microangiopathy has been accepted for filing by the FDA. The BLA has been granted Priority Review with an **FDA action date of July 17, 2021**. FDA also indicated in its filing letter that they are not planning to hold an advisory committee meeting to discuss the BLA.

- Narsoplimab is a human IgG4 antibody that targets mannan-binding lectin-associated serine protease-2.

On January 21, 2021, Incyte announced that the FDA has accepted for Priority Review its Biologics BLA for retifanlimab as a potential treatment for adult patients with locally advanced or metastatic squamous cell carcinoma of the anal canal who have progressed on, or who are intolerant of, platinum-based chemotherapy. **FDA's target action date for retifanlimab is July 25, 2021.**

- Retifanlimab is a humanized IgG4 antibody that targets programed cell death protein-1.

On January 29, 2021, Biogen and Eisai Co., Ltd. announced that the FDA has extended the review period by three months for the BLA for aducanumab, an investigational treatment for Alzheimer's disease. **FDA's target action date is June 7, 2021.**

- Aducanumab (BIIB037) is a human IgG1 monoclonal antibody targeting amyloid beta.

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February 1 - 15, 2021

COVID-19 intervention news

Rockefeller University mAbs licensed by BMS

On February 3, 2021, Bristol Myers Squibb and The Rockefeller University announced that they entered into a definitive agreement under which **BMS has been granted a global exclusive license to develop, manufacture and commercialize Rockefeller's novel monoclonal antibody (mAb) duo** treatment that neutralizes the SARS-CoV-2 virus for therapy or prevention of COVID-19. The Phase 1 **NCT04700163** open label, dose-escalation study of the safety and pharmacokinetics of a combination of C144-LS and C135-LS in healthy volunteers was started in January 2021.

- The two complementary antibodies target the SARS-CoV-2 spike protein and have shown activity against several known SARS-CoV-2 mutants. The mAbs' extended half-life was enabled via Xencor's Fc engineering technology.

Phase 3 study of CPI-006 started

On February 2, 2021, details were posted on clinicaltrials.gov for a Phase 3 placebo-controlled study (**NCT04734873**) of CPI-006 plus standard of care versus placebo plus standard of care in mild to moderately symptomatic hospitalized Covid-19 patients. Participants who receive drug will be administered CPI-006 2 mg/kg up to a maximum dose of 200 mg plus standard of care. Sponsored by Corvus Pharmaceuticals, Inc., the study is recruiting patients and has a primary completion date in December 2021.

- CPI-006 is a humanized IgG1 antibody that targets CD73. Administration of the mAb is anticipated to increase COVID-19 antibody production via B cell activation, and may reduce severity and duration of infection.

Emergency use of new mAbs authorized in South Korea and the US

On February 5, 2021, Celltrion Group announced that the **Korean Ministry of Food and Drug Safety granted a Conditional Marketing Authorisation (CMA) for the emergency use of regdanvimab** (CT-P59). The CMA allows for emergency use of CT-P59 in adult patients aged 60 years and over, or with at least one underlying medical condition (cardiovascular, chronic respiratory disease, diabetes, high blood pressure) with mild symptoms of COVID-19, and adult patients with moderate symptoms of COVID-19.

- Regdanvimab is a human mAb that targets SARS-CoV-2 spike protein.

On February 9, 2021, the U.S. **Food and Drug Administration issued an emergency use authorization for bamlanivimab and etesevimab** administered together for the treatment of mild to moderate COVID-19 in adults and pediatric who test positive for SARS-CoV-2 and who are at high risk for progressing to severe COVID-19. The authorized dosage of 700 milligrams bamlanivimab and 1400 milligrams etesevimab administered together is based on analyses of available preclinical, clinical, and virologic data, as well as pharmacokinetic and pharmacodynamic modeling,

- Developed by Eli Lilly and Company, bamlanivimab and etesevimab are mAbs that target overlapping regions of the SARS-CoV-2 spike protein.

Updates on non-COVID-19 interventions

INDs allowed by FDA

On February 4, 2021, **Heidelberg Pharma AG announced** that the FDA informed the company it is safe to proceed with the Phase 1/2a study with its investigational antibody HDP-101. The study will evaluate HDP101 for the treatment of multiple myeloma. The company expects the first patient to be enrolled and the first dose to be administered in the second quarter of 2021.

- HDP-101 is an antibody-drug conjugate (ADC) composed of an anti-B-cell maturation antigen antibody conjugated to the cytotoxic agent amanitin.

On February 8, 2021, **Catapult Therapeutics announced** the FDA has cleared the Investigational New Drug application for its lead product candidate, CAP-100. The planned Phase 1 clinical study (NCT04704323) will investigate the safety and efficacy of increasing doses of CAP-100 in relapsed or refractory patients to at least two prior standard systemic treatment regimens for chronic lymphocytic leukemia or small lymphocytic lymphoma and having no available therapies known to provide clinical benefit.

- CAP-100 is a humanized antibody targeting chemokine receptor CCR7, which is essential to migration of immune cells to lymphoid organs and is over-expressed in hematological malignancies with lymph node involvement.

Early-stage clinical studies started

On February 12, 2021, details were posted on clinicaltrials.gov for a first-in-human Phase 1/2a open-label, dose-escalation, multicenter, consecutive-cohort, clinical trial (**NCT04752826**) of BI-1808 as a single agent and in combination with pembrolizumab in subjects with advanced malignancies. Sponsored by BioInvent International AB, the study is recruiting patients. Estimated enrollment is 100 patients, and the estimated primary completion date is December 2024.

- BI-1808 is a human IgG1 mAb that targets tumor necrosis factor receptor 2.

On February 3, 2021, details were posted on clinicaltrials.gov for a Phase 2 clinical trial (**NCT04736823**) of AK112 in combination with chemotherapy in patients with non-small cell lung cancer (NSCLC). Sponsored by Akeso, the study is recruiting patients. Estimated enrollment is 206 patients, and the estimated primary completion date is January 2023.

- AK112 is a bispecific antibody that targets PD-1 and VEGF.

Late-stage clinical studies started

On February 4, 2021, details were posted on clinicaltrials.gov for a Phase 3 multicenter, randomized, double-blind study (**NCT04738487**) of vibostolimab (MK-7684) with pembrolizumab as a coformulation (MK-7684A) versus pembrolizumab monotherapy as first line treatment for participants with PD-L1 positive metastatic NSCLC. The coformulation is composed of vibostolimab 200mg and pembrolizumab 200mg. Participants will receive the coformulation by intravenous infusion every 3 weeks for up to 35 administrations. Sponsored by Merck Sharp & Dohme Corp., the study is not yet recruiting patients. Estimated enrollment is 598 patients, and the estimated primary completion date is April 2025.

- Vibostolimab is a humanized, IgG1 mAb that binds TIGIT and blocks its interaction with its ligands, CD112 and CD155.

On February 10, 2021, details were posted on clinicaltrials.gov for a Phase 3 randomized, double-blind study (**NCT04746924**) of BGB-A1217 in combination with tislelizumab compared to pembrolizumab in patients with previously untreated, PD-L1-selected, and locally advanced, unresectable, or metastatic NSCLC. Patients randomized to the experimental arm of the study will receive tislelizumab 200 mg intravenously followed by BGB-A1217 900 mg intravenously once every 3 weeks. Sponsored by BeiGene, the study is not yet recruiting patients. Estimated enrollment is 605 patients, and the estimated primary completion date is November 2024.

- BGB-A1217 is a humanized, IgG1 mAb that binds TIGIT and blocks its interaction with its ligands, CD112 and CD155.

BLA for tisotumab vedotin submitted to FDA

On February 10, 2021, Genmab A/S and Seagen Inc. announced the **submission of a Biologics License Application (BLA) to the FDA seeking accelerated approval for tisotumab vedotin**. This BLA requests FDA approval of tisotumab vedotin for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. The submission is based on the results of the innovaTV 204 pivotal Phase 2 single-arm clinical trial evaluating tisotumab vedotin as monotherapy in this setting.

- Tisotumab vedotin is an ADC composed of a human IgG1 antibody targeting tissue factor conjugated to the microtubule-disrupting agent monomethyl auristatin E via a protease-cleavable linker.

First approval granted for evinacumab

On February 11, 2021, the US **FDA approved Evkeeza (evinacumab-dgnb)** injection as an add-on treatment for patients aged 12 years and older with homozygous familial hypercholesterolemia, a genetic condition that causes severely high cholesterol. Evkeeza received orphan drug and breakthrough therapy designations for this indication, and the biological license application received a priority review.

- Evinacumab is a human IgG4k antibody targeting angiopoietin-like 3 (ANGPTL3), which regulates the metabolism of plasma lipids, including low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides. The antibody was derived from Regeneron's Velocimmune® technology platform, and includes a stabilizing mutation in the hinge region to minimize half-antibody formation.

Attending a virtual meeting soon?

Members of The Antibody Society save up to 20% on registration fees to attend:

World ADC Europe, March 8-11, 2021

- Use code TABS10 for a 10% discount

FcRn-Targeted Therapies for Autoimmune Disorders Summit, March 23-25, 2021

- Use code ABS10 for a 10% discount

PEGS Boston, May 11-13, 2021

- Use code TAS20 for a 20% discount

Antibody News You Should Know

February 15 - March 1, 2021

The Antibody Society
Webinar Series

IONTAS

TITLE: DEEP MINING OF EARLY ANTIBODY RESPONSE IN COVID-19 PATIENTS YIELDS POTENT NEUTRALIZERS AND REVEALS HIGH LEVEL OF CONVERGENCE

John McCafferty, CSO
IONTAS

Start Time: March 18, 2021 12:00 PM Eastern
11:00 AM Central, 10:00 AM Mountain, 9:00 AM Pacific

FairJourney Biologics Flow Eighteen30

COVID-19 intervention news

Antibody cocktails in preclinical development

On February 19, 2021, ImmunoPrecise Antibodies Ltd announced preliminary, **preclinical data in hamsters of their proprietary TATX-03 PolyTope antibody cocktail** against SARS-CoV-2. In the hamster model, treatment with TATX-03 resulted in complete clearance of detectable replication-competent virus from the lungs and throat of SARS-CoV-2 infected animals. The company intends to conduct what it anticipates will be the final IND-enabling studies, including non-human primate, dose-dependent evaluation of the TATX-03 antibody cocktail, in late Q2 2021.

- TATX-03 is a cocktail of four proprietary monoclonal antibodies (mAbs) directed against distinct regions of the SARS-CoV-2 spike protein.

On February 23, 2021, Aridis Pharmaceuticals, Inc. announced that it has **augmented its inhaled AR-711 monoclonal antibody (mAb) to COVID-19 with a second mAb (AR-713)** that is designed to neutralize newly emerging COVID-19 mutated variants, including those from South Africa, Brazil and Japan. The mAbs are engineered to be active for 6-12 months in the blood and formulated for effective delivery from commercially available nebulizers. Aridis is on track to initiate the program's Phase 1/2/3 clinical trial in 2H 2021.

- AR-711 and AR-713 are human IgG1 mAbs derived from B-cells of convalescent SARS-CoV-2 virus infected patients. The mAbs target the virus' receptor-binding domain (RBD) region of the spike protein at a distinct, unique site.

First Phase 1 study of ADG20 started

On February 16, 2021, Adagio Therapeutics, Inc. announced the **initiation of a Phase 1 clinical trial evaluating its lead anti-SARS-CoV-2 antibody product candidate, ADG20**. In this single ascending-dose study, healthy adult participants will either receive an intramuscular or intravenous dose of ADG20 or placebo. The clinical program for ADG20 is currently focused on outpatient populations, including an emphasis on addressing unmet needs in vulnerable groups such as the immune compromised and children.

- ADG20 is an anti-SARS-CoV-2 antibody that has been engineered to maximize its potential to avoid viral escape, which also enables ADG20 to target and neutralize coronaviruses that may emerge in the future.

EMA takes action on marketing applications for anti-SARS-CoV-2 antibodies

On February 26, 2021, the European Medicines Agency (EMA) announced that their

Committee for Medicinal Products for Human Use (CHMP) has started a **'rolling review' of data on regdanvimab** (also known as CT-P59 and Regkirona), which is being developed by Celltrion, for the treatment of COVID-19. Further information about COVID-19 treatments under evaluation by EMA can be **found here**. Regdanvimab was granted a conditional marketing authorization in Korea for treatment of COVID-19 and is seeking an Emergency Use Authorization (EUA) for this indication in the US, but is **not pursuing the development of regdanvimab as a prophylactic agent**, i.e., to prevent infection by SARS-CoV-2.

- Regdanvimab is a human mAb derived from B-cells of convalescent SARS-CoV-2 virus infected patients. It has been designed to attach to the spike protein of SARS-CoV-2.

On February 26, 2021, Roche confirmed that EMA's CHMP has issued a scientific opinion supporting the use of the investigational antibody cocktail, casirivimab and imdevimab, as a treatment option for patients with confirmed COVID-19 who do not require oxygen supplementation and who are at high risk of progressing to severe COVID-19. **CHMP's scientific opinion supports national decision making within EU member states** on the use of the antibodies before a formal authorization is granted during a public health emergency. Roche and Regeneron are collaborating on developing and manufacturing casirivimab and imdevimab; Roche will be responsible for distribution in Europe and other countries outside the US.

- Casirivimab and imdevimab (also known as REGN10933 and REGN10987, respectively) were designed by Regeneron scientists to block infectivity of SARS-CoV-2. The cocktail was authorized by FDA under an EUA for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Updates on non-COVID-19 interventions

Early-stage clinical studies starting

On February 17, 2020, details were posted on clinicaltrials.gov for a Phase 1 dose escalation and expansion study (**NCT04758767**) of CID-103 in patients with previously treated relapsed or refractory multiple myeloma. Sponsored by CASI Pharmaceuticals, Inc., the study's estimated enrollment is 60 patients and the estimated start date is March 1, 2021. CASI licensed the global rights to CID-103, which was originally developed by Tusk Therapeutics, Ltd, in April 2019.

- CID-103 (formerly known as TSK011010) is a novel anti-CD38 mAb.

On February 18, 2020, details were posted on clinicaltrials.gov for a Phase 1b/2 open-label study (**NCT04761198**) of the efficacy and safety of etigilimab (MPH313) administered in combination with nivolumab to subjects with locally advanced or metastatic solid tumors. Sponsored by Mereo BioPharma, the study is currently recruiting an estimated 125 participants. Mereo acquired etigilimab through its April 2019 merger with OncoMed.

- Etigilimab is a humanized IgG1 antibody targeting TIGIT.

Pivotal Phase 2 study of elranatamab started

On February 17, 2021, Pfizer Inc. announced that the **first participant has been dosed in the registration-enabling Phase 2 MagnetisMM-3 study (NCT04649359) of elranatamab** (PF-06863135) in patients with relapsed/refractory multiple myeloma. The study evaluates the efficacy and safety of elranatamab, administered subcutaneously, in patients with disease that is refractory to at least one agent in each of three major classes of medications approved for multiple myeloma. The study's estimated primary completion date is June 2022. Elranatamab has been granted Fast Track Designation by the U.S. Food and Drug Administration (FDA).

- Elranatamab is a bispecific antibody that targets B-cell maturation antigen on cancerous cells and CD3 on T cells, thereby directing the T cells and enabling them to kill the cancerous cell.

FDA grants priority review to Vicineum license application

On February 16, 2021, Sesen Bio announced **FDA accepted for filing the company's Biologics License Application (BLA) for Vicineum** for the treatment of high-risk, BCG-unresponsive non-muscle invasive bladder cancer (NMIBC), and granted the application Priority Review. The anticipated target Prescription Drug User Fee Act date for a decision on the BLA is August 18, 2021. The company expects to submit its Marketing Authorization Application to the EMA for Vicineum for the treatment of high-risk, BCG-unresponsive NMIBC in 1-2 months.

- Vicineum (oportuzumab monatox) is an immunotoxin composed of a humanized single-chain antibody fragment specific for the epithelial cell adhesion molecule antigen linked to ETA(252-608) Pseudomonas exotoxin.

CHMP adopts positive opinion of dostarlimab for endometrial cancer

On February 26, 2021, GlaxoSmithKline plc announced EMA's **CHMP adopted a positive opinion recommending dostarlimab** for use as monotherapy in women with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer who have progressed on or following prior treatment with a platinum containing regimen. If approved by the European Commission, dostarlimab would be the first anti-PD-1 therapy approved for endometrial cancer in Europe.

- Dostarlimab is an anti-programmed death-1 (PD-1) monoclonal antibody.

Voluntary withdrawal of durvalumab indication in advanced bladder cancer in the US

On February 22, 2021, AstraZeneca announced the **voluntary withdrawal of the Imfinzi (durvalumab) indication in the US for previously treated adult patients**

with locally advanced or metastatic bladder cancer. FDA granted accelerated approval of durvalumab for locally advanced or metastatic urothelial carcinoma on May 1, 2017. Continued approval was contingent on results from the DANUBE Phase 3 trial in the 1st-line metastatic bladder cancer setting, which did not meet its primary endpoints in 2020. The withdrawal is aligned with FDA guidance for evaluating indications with accelerated approvals that did not meet post-marketing requirements. This withdrawal does not affect the indication outside the US and does not affect other approved Imfinzi indications within or outside the US.

- Durvalumab is an anti-PD-L1 human IgG1 with a constant domain that contains three point mutations that reduce binding to C1q and the Fc gamma receptors. It is currently approved in the US for non-small cell lung cancer and small cell lung cancer.

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March 1 - 15, 2021

The Antibody Society
Webinar Series

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Start Time: March 18, 2021 12:00 PM Eastern
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FairJourney Biologics Flow Eighteen30

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John McCafferty, CSO
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COVID-19 intervention news

Positive early-stage clinical study results for MP0420

On March 9, 2021, Molecular Partners AG and its collaborator Novartis announced initial **results from its ongoing Phase 1 study of its first tri-specific COVID-19 antiviral DARPin® therapeutic, ensovibep** (MP0420), in healthy volunteers. Ensovibep was seen to be safe and well tolerated, with no significant adverse events reported, and preliminary results showed extended exposure of the DARPin® candidate in serum, with a half-life of 2-3 weeks. The companies plan to start a Phase 2/3 global registration study early in the second quarter of 2021.

- Ensovibep incorporates three SARS-CoV-2-binding DARPin® domains and a half-life enhancing DARPin domain that binds to human serum albumin.

Positive late-stage clinical study results for bamlanivimab and etesevimab

On March 10, 2021 Eli Lilly and Company announced new data from the randomized, double-blind, placebo-controlled **BLAZE-1 Phase 3 study, demonstrating bamlanivimab (LY-CoV555) 700 mg and etesevimab (LY-CoV016) 1400 mg** together significantly reduced COVID-19-related hospitalizations and deaths in high-risk patients recently diagnosed with COVID-19. These results provide additional efficacy and safety data that support the use of the dose recently granted Emergency Use Authorization by the U.S. Food and Drug Administration (FDA). The European Medicines Agency's human medicines committee (CHMP) has started a **'rolling review' of data on the antibodies bamlanivimab and etesevimab**.

- Bamlanivimab and etesevimab are human IgG1 antibodies that target the SARS-CoV-2 spike protein.

Updates on VIR-7831 in late-stage ACTIV-3 and COMET-ICE studies

On March 3, 2021, Vir Biotechnology, Inc. and GlaxoSmithKline plc announced that the Data and Safety Monitoring Board for the **ACTIV-3 trial evaluating VIR-7831 (sotrovimab)** in hospitalized adults with COVID-19 has recommended that the VIR-7831 arm of the trial be closed to enrolment while the data mature. Sensitivity analyses of the available data raised concerns about the magnitude of potential benefit in this patient population.

On March 10, 2021 , Vir Biotechnology, Inc. and GlaxoSmithKline plc announced that the Data Monitoring Board for the **Phase 3 COMET-ICE trial evaluating VIR-7831** (GSK4182136) as monotherapy for the early treatment of COVID-19 in adults at high risk of hospitalization be stopped for enrolment due to evidence of profound efficacy. An 85% reduction in hospitalization or death was observed. Vir and GSK plan to immediately seek Emergency Use Authorization in the US and authorizations in other countries.

- Sotrovimab is a human IgG1 antibody that targets the SARS-CoV-2 spike protein.

BRII-196 and BRII-198 will not progress in late-stage ACTIV-3 study

On March 3, 2021, Brii Biosciences announced that its antibodies **BRII-196 and BRII-198 failed to meet pre-specified efficacy criteria** permitting expansion into the Phase 3 component of ACTIV-3. NIH's ongoing COVID-19 Therapeutic Interventions and Vaccines (ACTIV-3) master protocol is examining the clinical safety and efficacy of investigational agents, including the combination therapy of BRII-196 and BRII-198, relative to current standard of care (SOC) therapy in hospitalized patients with more severe COVID-19.

- BRII-196 and BRII-198 are human IgG1 antibodies that target the SARS-CoV-2 spike protein.

Updates on non-COVID-19 interventions

Amgen acquires Five Prime Therapeutics

On March 4, 2021, Amgen and Five Prime Therapeutics announced an agreement under which **Amgen will acquire Five Prime Therapeutics**. Five Prime's lead asset, bemarituzumab, is a first-in-class, Phase 3-ready antibody with positive data from a randomized, placebo-controlled Phase 2 study in frontline advanced gastric or gastroesophageal junction cancer. **As announced in January 2021**, clinically meaningful improvements in progression-free survival, overall survival, and overall response rate were observed in this Phase 2 study. Five Prime Therapeutics granted an exclusive license to Zai Lab Limited to develop and commercialize bemarituzumab in Greater China, and Zai Lab collaborated with Five Prime Therapeutics on the Phase 2 FIGHT trial in Greater China.

- Bemarituzumab is a humanized, glyco-engineered IgG1 antibody that targets a splice variant of the fibroblast growth factor receptor (FGFR2b). The FGF/FGFR pathway is implicated in the development and growth of cancer cells.

First-in-human studies starting soon

On March 2, 2021, **Sorrento Therapeutics, Inc. announced** that the FDA cleared Sorrento's internally developed anti-CD47 monoclonal antibody, STI-6643, for an initial clinical trial. The initial clinical trial will be a basket trial that will include patients with selected relapsed or refractory malignancies.

- STI-6643 is a human monoclonal antibody targeting CD47, a ubiquitously-expressed glycoprotein of the immunoglobulin superfamily that plays a critical role in self-recognition.

On March 3, 2021, **Xentria Inc. announced** that it had submitted an Investigational New Drug application to the FDA that supports a proposed indication for XTMAB-16 for treatment of sarcoidosis, a potentially life-threatening inflammatory disease. The first clinical trial could be started as early as Q2 2021. FDA granted XTMAB-16 Orphan Drug Designation in November 2020.

- XTMAB-16 is a chimeric human-murine IgG1κ monoclonal antibody that targets tumor necrosis factor.

On March 5, 2021, details were posted on clinicaltrials.gov for a first-in-human study (**NCT04784312**) of 9MW1411 in healthy subjects. Sponsored by Mabwell (Shanghai) Bioscience Co., Ltd., this study has an estimated start date in April 2021.

- 9MW1411 is a recombinant humanized anti-Staphylococcus aureus α-toxin monoclonal antibody.

On March 10, 2021, **LAVA Therapeutics B.V., a biotechnology company developing bispecific gamma-delta T cell engagers (bs TCE), announced** that a

poster featuring lead clinical candidate LAVA-051 will be presented at the virtual American Association for Cancer Research Annual Meeting, which will be held April 10-15, 2021. The company plans to start a Phase 1/2a study of LAVA-051 in hematologic malignancies in 1H 2021.

- LAVA-051 is a humanized gamma-delta bsTCE that targets CD1d and the Vδ2 domain of the T cell receptor. It is the first antibody-based compound targeting CD1d to activate both Vγ9Vδ2-T and type 1 NKT cells.

First Phase 2 study of bispecific antibody combination starting soon

On March 8, 2021, details were posted on clinicaltrials.gov for a 3-arm, randomized, blinded, active-controlled, Phase 2 study (**NCT04785820**) of RO7121661 and RO7247669 compared with nivolumab in participants with advanced or metastatic squamous cell carcinoma of the esophagus. Sponsored by Hoffmann-La Roche, the study's estimated start date is April 19, 2021.

- RO7121661 is a bispecific antibody targeting the immune system checkpoints PD1 and TIM3.
- RO7247669 is a bispecific antibody targeting the immune system checkpoints PD1 and LAG3.

First Phase 3 study of cosibelimab starting soon

On March 8, 2021, details were posted on clinicaltrials.gov for a Phase 3 Study (**NCT04786964**) of cosibelimab in combination with platinum+pemetrexed chemotherapy in subjects with first-line metastatic non-squamous non-small cell lung cancer. Sponsored by Checkpoint Therapeutics, Inc., this study has an estimated start date in June 2021.

- Cosibelimab is a human IgG1 monoclonal antibody that binds to programmed cell death protein-1 ligand (PD-L1) and blocks its interactions with the PD-1 and B7.1 receptors.

Biologics license application submission for toripalimab started

On March 3, 2021, Shanghai Junshi Biosciences Co., Ltd. and Coherus Biosciences, Inc. announced the i**nitiation of the rolling submission of the Biologics License Application (BLA) for toripalimab** to the FDA for the treatment of recurrent or metastatic nasopharyngeal carcinoma. Toripalimab (Tuoyi)was granted Breakthrough Therapy Designation by the FDA for the treatment of this disease. On December 17, 2018, toripalimab obtained a conditional approval from China's National Medical Products Administration for the second-line treatment of unresectable or metastatic melanoma.

- Toripalimab is a humanized IgG4 antibody that targets PD-1.

BLA for efgartigimod accepted by FDA

On March 4, 2021, argenx announced that the **BLA for efgartigimod was accepted for review by FDA** and the company was on track with commercial and regulatory preparations in the U.S., Japan, the EU and China. The BLA for IV efgartigimod for treatment of generalized myasthenia gravis has with action date set for December 17, 2021 under the Prescription Drug User Fee Act.

- Efgartigimod is an IgG1 Fc designed for increased affinity for FcRn. It competes with IgG to occupy FcRn and reduce overall IgG recycling.

Antibody News You Should Know

March 15 - April 1, 2021

COVID-19 intervention news

Anti-SARS-CoV-2 antibodies shown to neutralize viral variants

On March 22, 2021, IONTAS Limited and FairJourney Biologics S.A announced the **identification of neutralizing antibodies that bind to multiple emerging SARS-CoV-2 variants**. Generated from a combination of phage display technology and B-cell receptor repertoire sequencing of hospitalized COVID-19 patients, the potent virus-neutralizing antibodies have distinct mechanisms of action. The companies are seeking partners to help develop these antibodies.

On March 25, 2021, IMMUNOPRECISE ANTIBODIES LTD. announced the **identification of anti-SARS-CoV-2 antibody 23-H7**. Preclinical data obtained to date indicates provides strong, protective anti-viral effects in SARS-CoV-2-infected Syrian hamsters via an uncommon mechanism of action. 23-H7, which does not bind at the RBD/ACE2 interface, maintained binding to the full (cell-associated) spike trimer of emerging SARS-CoV-2 variants of concern B.1.1.7

(UK), B.1.351 (S. African), and P.1 (Brazilian).

First-in-human clinical studies to start soon

On March 16, 2021, **CORAT Therapeutics GmbH announced** that they had obtained regulatory authorization for a clinical Phase 1b/2 trial (**NCT04674566**) that will evaluate COR-101, which has been shown to bind variants of SARS-CoV-2, including the N501Y/E484K (B.1.1.7.), N439K, and E484K variants. This randomized, double-blind, placebo-controlled, parallel-group, first-in-human study will assess the effects of COR-101 in hospitalized patients with moderate to severe COVID-19. The estimated study start date is April 1, 2021.

- COR-101 is a SARS-CoV-2 neutralizing human antibody

On March 16, 2021, details were posted on clinicaltrials.gov for a Phase 1, first-in-human, randomized, single ascending dose study (**NCT04801056**) of TB006 in outpatient patients with mild to moderate COVID-19. Dosages of 10 mg/kg to 50 mg/kg will be investigated in patients with the disease. The study sponsor is TrueBinding, Inc. An estimated 27 patients will be included in the study, which has an estimated start date in March 2021.

- TB006 is an anti-inflammatory and anti-fibrotic anti-TB-L1 monoclonal antibody that may reduce the severity of underlying diseases in COVID-19 patients. TB-L1 is a TIM-3 ligand.

Late-stage clinical study of BI 767551 to start soon

On March 30, 2021, details were posted on clinicaltrials.gov for a Phase 2/3 seamless, randomized, double-blind, placebo-controlled, parallel-group, group-sequential study (**NCT04822701**) to evaluate the effects of BI 767551 in symptomatic, non-hospitalized adults with mild to moderate COVID-19. Both infusion and inhaled formulations of BI 767551 will be evaluated. The study sponsor is Boehringer Ingelheim. An estimated 1440 patients will be included in the study, which has an estimated start date in April 2021.

- BI 767551 is a human mAb targeting the SARS-CoV-2 virus.

Positive Phase 3 study results for lenzilumab

On March 29, 2021, Humanigen, Inc announced **positive topline results from its Phase 3 clinical trial evaluating the efficacy and safety of lenzilumab** in patients hospitalized with COVID-19. Trial results showed that patients who received lenzilumab and other treatments, including steroids and/or remdesivir, had a 54% greater relative likelihood of survival without the need for invasive mechanical ventilation compared with patients receiving placebo and other treatments. The company plans to submit an application for Emergency Use Authorization (EUA) to the Food and Drug Administration (FDA) as soon as possible.

- Lenzilumab is a Humaneered® monoclonal antibody that targets human granulocyte macrophage-colony stimulating factor.

EUA application submitted for anti-SARS-CoV-2 VIR-7831

On March 26, 2021, GlaxoSmithKline plc and Vir Biotechnology, Inc. announced the submission of an **application to the FDA requesting an EUA for VIR-7831 (GSK4182136)**, an investigational dual-action SARS-CoV-2 monoclonal antibody, for the treatment of adults and adolescents (aged 12 years and older weighing at least 40 kg) with mild-to-moderate COVID-19 who are at risk for progression to hospitalization or death. GSK and Vir are engaging in discussions with the European Medicines Agency (EMA) and other global regulators to make VIR-7831 available to patients with COVID-19 as soon as possible.

Updates on non-COVID-19 interventions

Preclinical data for anti-GLP-1R antibodies published

On March 22, 2021, **Twist Bioscience Corporation announced positive preclinical data** demonstrating that glucagon-like peptide-1 receptor (GLP-1R) antibodies identified from its proprietary G-protein coupled receptor libraries showed potent blood glucose control. Many of the GLP-1R antibodies discovered were GLP-1R antagonists, which have the ability to prevent hypoglycemia incidents in congenital hyperinsulinism and post-bariatric hyperinsulinism. Twist Biopharma also created an agonist antibody, TB59-2, by fusing GLP-1 peptide to the light chain of a non-functional GLP-1R-specific antibody. In vivo studies indicate that TB59-2 has potential to be used to treat type 2 diabetes with a once-weekly dose. The study results were **published in *mAbs*.**

First Phase 1 of ADG126 started

On March 16, 2021, Adagene Inc. announced the first patients have been dosed in its global **Phase 1 clinical trial of ADG126** for the treatment of various advanced solid tumors. The global Phase 1 open-label, dose-escalation clinical trial is investigating the tolerability and anti-tumor activity of ADG126 in patients with advanced/metastatic tumors in multiple clinical sites in Australia. Adagene has also received approval from the FDA to initiate the Phase 1 clinical trial (NCT04645069) of ADG126 in the United States. The dose escalation trial will test five doses at 0.1, 0.3, 1.0, 3.0 and 10 mg/kg, with dose-limiting toxicities evaluation for 3 weeks.

- ADG126, a human, antagonistic monoclonal antibody targeting a novel epitope of CTLA-4, is Adagene's lead SAFEbody™ product candidate.

Enfortumab vedotin undergoing review by EMA

On March 26, 2021, Astellas Pharma Inc. and Seagen Inc. announced that a **marketing authorization application (MAA) for enfortumab vedotin** (PADCEV) was accepted by the EMA. The MAA requests review of enfortumab vedotin for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and who have received a platinum-

containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting. Enfortumab vedotin will be reviewed under accelerated assessment.

- Enfortumab vedotin is an antibody-drug conjugate (ADC) composed of a human IgG1 antibody that targets Nectin-4 conjugated to monomethyl auristatin E. It was approved by FDA for bladder cancer in December 2019.

Sacituzumab govitecan undergoing review by EMA

On March 23, 2021, Gilead Sciences, Inc. announced that the **EMA validated the MAA for sacituzumab govitecan-hziy** (Trodelvy®) for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) who have received at least two prior therapies, including at least one prior therapy for locally advanced or metastatic disease. In April 2020, Trodelvy® received accelerated approval by the U.S. Food and Drug Administration (FDA) to treat adult patients with metastatic TNBC who have received at least two prior therapies for metastatic disease.

- Sacituzumab govitecan is an ADC composed of a humanized IgG1 antibody targeting TROP-2 conjugated to SN38, the active metabolite of irinotecan.

Majority of FDA Advisory Committee members vote against tanezumab

On March 25, 2021, Pfizer Inc. and Eli Lilly and Company announced the outcome of the FDA Joint Arthritis Advisory Committee and Drug Safety and Risk Management Advisory Committee on tanezumab. Tanezumab 2.5 mg administered subcutaneously every eight weeks is being evaluated for the treatment of moderate-to-severe osteoarthritis pain in adult patients for whom use of other analgesics is ineffective or not appropriate. There was a single voting question focused on whether the proposed risk evaluation and mitigation strategy for tanezumab will ensure its benefits outweigh its risks, and **the Committee**

voted 1 in favor and 19 against. Advisory Committee recommendations are not binding, but FDA commonly follows the advice.

- Tanezumab is a humanized IgG2 monoclonal antibody that targets nerve growth factor.

Attending a virtual meeting soon?

The Antibody Society members save up to 20% on registration fees to attend:

PEGS Boston, May 11-13, 2021

- Use code TAS20 for a 20% discount

Antibody Engineering & Therapeutics Europe, June 8-10, 2021

- Use code Antibody15 for a 15% discount

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Antibody Industrial Symposium, June 22-25, 2021