Antibody News You Should Know

April 1 - 15, 2021

COVID-19 intervention news

NIH evaluating anti-CD14 therapy in COVID-19

On April 13, 2021, the National Institute of Allergy and Infectious Diseases (NIAID) announced the start of the **Phase 2 COVID-19 anti-CD14 Treatment Trial (NCT04391309**; CaTT), which will evaluate the effects of IC14 in 300 hospitalized adult COVID-19 patients. The study is sponsored by NIAID, and Implicit Bioscience Ltd. will supply IC14. Results are expected in early 2022.

 IC14 (atibuclimab) is a chimeric IgG4 monoclonal antibody that binds to CD14 with high affinity and inhibits signaling via membrane and soluble CD14, thereby potentially blocking hyperactive inflammatory responses.

Endpoints met in clinical studies of anti-SARS-CoV-2 antibodies

On April 12, 2021, Regeneron Pharmaceuticals, Inc. announced **positive results from a Phase 3 trial (2069A)** assessing the ability of REGEN-COV[™] (casirivimab with imdevimab) to reduce the risk and burden of COVID-19 infection among household contacts of SARS-CoV-2 infected individuals. The trial, which was jointly run with the NIAID, met its primary and key secondary endpoints, showing that REGEN-COV 1,200 mg administered subcutaneously reduced the risk of symptomatic infections by 81% in those who were not infected when they entered the trial.

Also on April 12, 2021, Regeneron Pharmaceuticals, Inc. announced **positive data from a Phase 3 trial (2069B)** of recently infected asymptomatic COVID-19 patients that evaluated REGEN-COV[™] 1,200 mg administered via subcutaneous administration. REGEN-COV reduced the overall risk of progressing to symptomatic COVID-19 by 31% (primary endpoint), and by 76% after the third day. The trial also demonstrated that REGEN-COV shortened symptom duration and markedly reduced viral levels.

• Casirivimab and imdevimab are human IgG1 antibodies that target the Spike protein of SARS-CoV-2.

Updates on non-COVID-19 interventions

New early-stage clinical studies

On April 1, 2021, details were posted on clinical trials.gov for an open-label, multicenter, Phase 1/2 trial (**NCT04824794**) of GEN3014 in relapsed or refractory multiple myeloma and other hematologic malignancies. The Phase 1 part of the study will determine the maximum tolerated dose (MTD) and the recommended Phase 2 dose (RP2D), as well as establish the safety profile of GEN3014. The study's estimated enrollment is 152 patients and the estimated primary completion date is in March 2023.

 GEN3014 (HexaBody®-CD38) is a novel, hexamerization-enhanced human IgG1 targeting CD38 with superior complement-dependent cytotoxicity activity, in addition to other effector mechanisms. In 2019, Genmab A/S entered into an exclusive worldwide license and option agreement with Janssen Biotech, Inc. to develop and commercialize GEN3014.

On April 6, 2021, **I-Mab and ABL Bio announced** the first patient had been dosed in a Phase 1 study of TJ-L14B/ABL503. This study (**NCT04762641**) is an open-label, multi-center, dose-escalation and dose-expansion study to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD),

preliminary antitumor activity, MTD and/or RP2D of TJ-L14B/ABL503 in locally advanced or metastatic solid tumors. This study will enroll an estimated 36 patients and the estimated primary completion date is in June 2023.

 TJ-L14B/ABL503 is a PD-L1-based bispecific antibody with the PD-L1 arm as the tumor-dependent T-cell activator and the 4-1BB arm as the conditional T cell activator upon tumor engagement.

On April 9, 2021, details were posted on clinical trials.gov for a Phase 1 (NCT04839991) open-label, dose escalation and expansion trial to investigate the safety, PK and PD of CB307 in patients with prostate specific membrane antigen (PSMA)-positive advanced and/or metastatic solid tumors. Sponsored by Crescendo Biologics Ltd. this study will enroll an estimated 50 patients and the estimated primary completion date is in June 2023.

 CB307 is a novel tri-specific Humabody therapeutic targeting CD137 (4-1BB), PSMA, and human serum albumin.

On April 13, 2021, details were posted on clinicaltrials.gov for an open-label, multi-center, Phase 1/2 dose escalation and expansion study (**NCT04843709**) to assess the safety, tolerability, anti-tumor activity and pharmacokinetics of MRG004A in patients with tissue factor positive advanced or metastatic solid tumors. Sponsored by Shanghai Miracogen Inc., this study will enroll an estimated 181 patients and the estimated primary completion date is in April 2024.

• MRG004A is an antibody-drug conjugate (ADC) that targets an undisclosed antigen.

Fast Track designation granted to pamrevlumab

On April 12, 2021, FibroGen, Inc. announced that the U.S. Food and Drug Administration (FDA) granted **Fast Track designation for pamrevlumab** for the treatment of patients with Duchenne muscular dystrophy (DMD). Pamrevlumab is currently being evaluated in two Phase 3 trials for the treatment of DMD, as well as Phase 3 studies for the treatment of locally advanced unresectable pancreatic cancer and idiopathic pulmonary fibrosis.

• Pamrevlumab is a human IgG1 antibody that targets connective tissue growth factor, a biological mediator in fibrotic and proliferative disorders.

BLA for tisotumab vedotin receives Priority review

On April 09, 2021, Genmab A/S and Seagen Inc. announced that the **FDA has** accepted for Priority Review the Biologics License Application seeking accelerated approval for tisotumab vedotin for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. The FDA's target action date is Oct 10, 2021.

 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. The targeted antigen is a cell-surface protein expressed on multiple solid tumors including cervical cancer, and is associated with tumor growth, angiogenesis, metastasis and poor prognosis.

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Antibody News You Should Know

April 15 - May 1, 2021



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COVID-19 intervention news

First-in-human study started

On April 22, 2021, CORAT Therapeutics GmbH announced the **start of a clinical trial with COR-101** for treatment of COVID-19 in hospitalized patients. The Phase 1b/2 trial (NCT04674566) is being conducted at five study centers in Germany.

• COR-101 is an anti-SARS-CoV-2 human IgG monoclonal antibody derived from B cells of recovered COVID-19 patients.

Phase 2/3 studies started

On April 21, 2021, SAB Biotherapeutics announced that the first patient has

been dosed in its Phase 2/3 study evaluating the safety and efficacy of SAB-185 as part of the NIH's ACTIV-2 (NCT04518410) master protocol. The trial is a randomized, double-blind, adaptive study that will examine the clinical safety and efficacy of SAB-185 in addition to standard of care in non-hospitalized patients with mild to moderate COVID-19 at risk for disease progression. Each sub-study in ACTIV-2 shares the placebo group and plans to enroll 110 participants. SAB-185 is administered intravenously and will be evaluated in a high- and low-dose arm.

• SAB-185 is a human, specifically targeted and broadly neutralizing polyclonal antibody therapeutic candidate for COVID-19.

On April 26, 2021, details for Adagio's Phases 2/3 study (**NCT04859517**) of ADG20 were posted on clinicaltrials.gov. This study will evaluate the efficacy and safety of ADG20 in the prevention of COVID 19. An estimated 6412 participants who will receive a single intramuscular dose of ADG20 are currently being recruited. The estimated primary completion date is July 2022.

• ADG20 is a half-life engineered, anti-SARS-CoV-2 human IgG monoclonal antibody derived from the B cell of a 2003 SARS survivor.

EMA review of VIR-7831 for COVID-19

On April 15, 2021, GlaxoSmithKline plc and Vir Biotechnology, Inc. today announced that the **European Medicines Agency has started a review of VIR-7831 (GSK4182136)** for the treatment of adults and adolescents (aged 12 years and over and weighing at least 40 kg) with COVID-19 who do not require oxygen supplementation and who are at high risk of progressing to severe COVID-19. EMA's review will include data from an interim analysis of efficacy and safety data from the Phase 3 COMET-ICE trial. Results of an interim analysis, based on data from 583 randomized patients, demonstrated an 85% (p=0.002) reduction in hospitalization or death in those receiving VIR-7831 compared to placebo, the primary endpoint of the trial. VIR-7831 is an anti-SARS-CoV-2 monoclonal antibody that incorporates Xencor's Xtend[™] technology and has been designed to achieve high concentration in the lungs and to have an extended half-life.

FDA revokes bamlanivimab's emergency use authorization

On April 16, 2021, the US Food and Drug Administration (FDA) revoked the emergency use authorization that allowed bamlanivimab, when administered alone, to be used for the treatment of mild-to-moderate COVID-19 in adults and certain pediatric patients. This action was based on the sustained increase of SARS-CoV-2 viral variants that are resistant to bamlanivimab when used as monotherapy. The combination of bamlanivimab and etesevimab, administered together, has emergency use authorization for the same uses as previously authorized for bamlanivimab alone.

• Bamlanivimab is a human anti-SARS-CoV-2 antibody.

Updates on non-COVID-19 interventions

First Phase 1 studies pending or started

On April 19, 2021, XBiotech Inc. announced that the **FDA granted permission to commence clinical trials with XB2001** in combination with ONIVYDE + LV + 5-FU chemotherapy regimen in patients with advanced pancreatic cancer. This novel drug approach may both antagonize the biology of the tumor and mitigate chemotherapy-related toxicities. The Phase 1/2 study (NCT04825288) has an estimated enrollment of 69 participants and an estimated start date of April 19, 2021. • XB2001 is a human IgG4 antibody that potently neutralizes IL-1 α .

On April 20, 2021, Transcenta Holding announced that it has received **clearance of its investigational new drug application for TST005** from US FDA, allowing the initiation of a Phase 1 clinical trial in cancer patients. The study will have an innovative basket trial design; protocol details are not yet available.

 TST005 is composed of a high affinity PD-L1 antibody fused with an engineered TGF-β Receptor Type II protein in its C-terminal. The molecule lacks FcR binding activity, and thus has reduced FcR-mediated killing of PD-L1 expressing effector T cells.

On April 28, 2021, details were posted on clinicaltrials.gov for a Phase 1 study (**NCT04863287**) in healthy subjects to evaluate the safety and pharmacokinetics of 2217LS, which is an investigational antibody candidate for Lyme disease. This tick-borne illness occurs predominantly in the northeast and north-central portions of the United States.

• 2217LS is a human monoclonal antibody that targets the outer surface protein A of *Borrelia burgdorferi*.

On April 28, 2021, Xencor, Inc. announced that **the first subject has been dosed in a randomized, double-blind, placebo-controlled Phase 1 clinical study of XmAb564**, which is a potential treatment for patients with autoimmune diseases. The study will evaluate the safety and tolerability of XmAb564, administered subcutaneously in healthy adult volunteers.

 XmAb564 is a monovalent interleukin-2 Fc fusion protein, engineered to selectively activate and expand regulatory T cells. The molecule was engineered with reduced binding affinity for IL-2's beta receptor (CD122) and increased binding affinity for its alpha receptor (CD25).

Breakthrough Therapy designation for bemarituzumab

On April 19, 2021, **Amgen announced that the FDA granted Breakthrough Therapy Designation for bemarituzumab** (FPA144) as first-line treatment for patients with fibroblast growth factor receptor 2b (FGFR2b) overexpressing and human epidermal growth factor receptor 2-negative metastatic and locally advanced gastric and gastroesophageal adenocarcinoma in combination with modified FOLFOX6 (fluoropyrimidine, leucovorin, and oxaliplatin), based on an FDA-approved companion diagnostic assay showing at least 10% of tumor cells overexpressing FGFR2b. Bemarituzumab was originally developed by Five Prime Therapeutics, which was acquired by Amgen in March 2021.

• Bemarituzumab is a humanized, glyco-engineered IgG1 antibody that targets FGFR2b.

Marketing applications submitted

On April 19, 2021, Agenus Inc. announced the **submission of a Biologics License Application (BLA) to the FDA for the accelerated approval of balstilimab** for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. Overall data from a pivotal Phase 2 study of balstilimab showed response rates of 20% in PD-L1 positive tumors, 15% in all tumors (PD-L1 positive and negative), and a median duration of response of 15.4 months. FDA previously granted Fast Track designation for balstilimab in recurrent or metastatic cervical cancer.

• Balstilimab is a human IgG4 anti-PD-1 antagonist antibody that potently inhibits PD-1 binding to PD-L1 and PD-L2.

On April 22, 2021, Shanghai Henlius Biotech, Inc. announced that the **New Drug Application of serplulimab** injection (HLX10) for the treatment of unresectable or metastatic microsatellite instability-high solid tumors that fail to respond to the standard therapy, has been accepted by China's National Medical Products Administration and proposed to be granted priority review. • Serplulimab is a humanized IgG4 anti-PD-1 monoclonal antibody.

On April 27, 2021, Y-mAbs Therapeutics, Inc. announced that the company has **submitted its Marketing Authorization Application to the European Medicines Agency (EMA) for omburtamab** for the treatment of pediatric patients with central nervous system (CNS)/leptomeningeal metastasis from neuroblastoma. The company aims to resubmit a Biologics License Application for omburtamab to the FDA late in the second quarter or in the third quarter of 2021.

• Omburtamab is an IgG1 monoclonal antibody that targets B7-H3 and is radiolabeled before intraventricular CNS administration.

CHMP issues positive opinions for satralizumab and tralokinumab On April 22, 2021, EMA's Committee for Medicinal Products for Human Use **(CHMP) recommended the approval of ENSPRYNG® (satralizumab)** as the first subcutaneous treatment option for adults and adolescents from 12 years of age living with anti-aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorder, as a monotherapy or in combination with immunosuppressive therapy. The applicant for ENSPRYNG® is Roche. Satralizumab was approved by the FDA in August 2020.

• Satralizumab is a humanized IgG2 monoclonal antibody designed to have pH-dependent binding to soluble interleukin (IL)-6 receptor.

Also on April 22, 2021, the CHMP adopted a positive opinion, recommending the granting of a marketing authorization for the medicinal product Adtralza (tralokinumab), intended for the treatment of moderate-to-severe atopic dermatitis. The applicant for Adtralza is LEO Pharma A/S. FDA is reviewing a BLA for tralokinumab • Tralokinumab is a human IgG4 monoclonal antibody that inhibits IL-13 signaling.

FDA approves loncastuximab tesirine and dostarlimab

On April 22, 2021, the **FDA granted accelerated approval to Jemperli** (dostarlimab) for treating patients with recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing chemotherapy and whose cancers are deficient in their ability to repair DNA inside the cell, as determined by an FDA-approved test. FDA granted dostarlimab Priority Review and Breakthrough Therapy designations for this indication.

 Dostarlimab (TS-042, GSK4057190A) is an anti-PD-1 humanized IgG4k antibody generated by Anaptysbio under partnership with Tesaro, which was acquired by GlaxoSmithKline in 2019.

On April 23, 2021, the **FDA granted accelerated approval to loncastuximab tesirine-Ipyl (Zynlonta**, ADC Therapeutics SA) for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma. This marketing application was granted priority review and orphan drug designation by FDA. The review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment.

 Loncastuximab tesirine (ADCT-042) is an antibody-drug conjugate composed of an anti-CD19 humanized IgG1k antibody conjugated via a linker to pyrrolobenzodiazepine-dimer toxin that induces the killing of CD19-expressing malignant B cells.

Antibody News You Should Know

May 1-15, 2021



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COVID-19 intervention news

LY-CoV1404 (LY3853113) now in clinical trial

On May 4, 2021, AbCellera announced that a second antibody from its collaboration with Eli Lilly and Company, LY-CoV1404 (LY3853113), has entered a clinical trial in patients with mild-to-moderate COVID-19. Lilly has expanded its ongoing BLAZE-4 trial to evaluate LY-CoV1404 alone and together with other monoclonal antibodies.

 LY-CoV1404 is a SARS-CoV-2 spike glycoprotein receptor binding domain (RBD)-specific antibody identified from a convalescent COVID-19 patient.
LY-CoV1404 binds to a rarely mutated region of the SARS-CoV-2 spike protein and neutralizes all currently known variants of concern, including those first identified in the UK (B.1.1.7), South Africa (B.1.351), Brazil (P.1), California (B.1.426 and B.1.429), and New York (B.1.526).

Phase 3 study of XAV-19 started

On May 3, 2021, **XENOTHERA announced the start of EUROXAV**, a European clinical trial of its anti-COVID treatment, XAV-19. EUROXAV is a multi-center, double-blind Phase 3 trial that will recruit 722 patients with moderate COVID, hospitalized or monitored remotely. The trial will take place in Greece, Bulgaria, Romania, Spain and Turkey.

• XAV-19 is a protective anti-SARS-CoV-2 heterologous swine glycohumanized polyclonal antibody.

CERC-002 granted Fast Track designation

On May 11, 2021, Cerecor Inc. announced that the U.S. Food and Drug Administration (FDA) has granted **Fast Track designation to CERC-002** for treatment of hospitalized patients with COVID-19. The company has completed a double-blinded, placebo-controlled Phase 2 proof-of-concept study of CERC-002 in hospitalized COVID-19 patients with mild-to-moderate acute respiratory distress syndrome.

• CERC-002 is a human monoclonal antibody targeting LIGHT (tumor necrosis factor superfamily member 14, TNFSF14).

Updates on non-COVID-19 interventions

First-in-human studies due to start soon

On May 6, 2021, details were posted on clinicaltrials.gov for a Phase 1/2 dose-

escalation, safety and tolerability study (**NCT04875806**) of NC762 in subjects with advanced or metastatic solid tumors. Sponsored by NextCure, Inc., this study's estimated start date is in June 2021.

• NC762 is a monoclonal antibody that binds specifically to B7-H4, a protein expressed on multiple tumor types.

On May 11, 2021, details were posted on clinicaltrials.gov for a Phase 1 dose escalation and expansion study (**NCT04881045**) evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and antitumor activity of PF-07257876 in patients with advanced or metastatic tumors. Sponsored by Pfizer, this study's estimated start date is June 7, 2021.

• PF-07257876 is a bispecific antibody targeting CD47 and PD-L1.

On May 14, 2021, details were posted on clinicaltrials.gov for a Phase I/II, multicenter, single-arm, open-label study (**NCT04886765**) to evaluate the safety and efficacy of ALMB-0168 in patients with osteosarcoma. Sponsored by AlaMab Therapeutics (Shanghai) Inc., this study's estimated start date is in May 2021.

• ALMB-0168 is a humanized anti-connexin 43 monoclonal antibody.

First-in-human studies started

On May 03, 2021, **Merus N.V. announced** that the first patient has been treated in its Phase 1/2 dose escalation and expansion trial (**NCT04868877**) evaluating MCLA-129 for the treatment of patients with advanced non-small cell lung cancer (NSCLC) and other solid tumors.

 MCLA-129 is a human bispecific Biclonics[®] antibody that binds EGFR and c-MET.

On May 10, 2021, details were posted on clinicaltrials.gov for a Phase 1 study (**NCT04880291**) to evaluate the safety, tolerability, and pharmacokinetics of GFB-024 as a single dose in healthy overweight and obese participants and as

multiple doses in participants with type 2 diabetes mellitus. Sponsored by Goldfinch Bio, Inc., the study is recruiting an estimated 56 participants.

• GFB-024 peripherally acting Cannabinoid-1 receptor inverse agonist monoclonal antibody.

On May 14, 2021, details were posted on clinicaltrials.gov for a Phase 1 and 2a trial (**NCT04887259**) to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, immunogenicity and antitumor activity of LAVA-051 in patients with relapsed or refractory CD1d-positive chronic lymphocytic leukemia, multiple myeloma, and acute myeloid leukemia. Sponsored by Lava Therapeutics, the study is recruiting an estimated 55 participants.

• LAVA-051 is a humanized gamma-delta bispecific T cell engager that targets CD1d and the V δ 2 domain of the T cell receptor.

BLA for tezepelumab submitted

On May 10, 2021, Amgen announced that its partner **AstraZeneca submitted a Biologics License Application to the FDA for tezepelumab**, for patients with severe asthma. The submission is supported by positive clinical trial results from the PATHFINDER clinical program including the pivotal NAVIGATOR Phase 3 trial, the results of which results were recently **published in the New England Journal of Medicine**. In 2018, FDA granted Breakthrough Therapy Designation to tezepelumab for patients with severe asthma, without an eosinophilic phenotype.

• Tezepelumab is a human IgG2 antibody that targets thymic stromal lymphopoietin, an epithelial-cell–derived cytokine implicated in the pathogenesis of asthma.

Antibody News You Should Know

May 15 - June 1, 2021

AIRR Community Webinar Series

Fundamentals of the Immune System

Part 1: Organization of the immune system Thursday, June 3, 2021 11AM - 1PM ET

Part 2: The immune system in action Tuesday, June 15, 2021 11AM - 1PM ET



Presenter Jamie Scott, MD, PhD, Professor Emerita, Simon Fraser University, Canada

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COVID-19 intervention news

New anti-SARS-CoV-2 antibodies aim for the clinic

On May 17, 2021, Memo Therapeutics AG announced that **MTX-COVAB has shown efficacy** against both the original virus as well as the UK variant (B.1.1.7). Memo is now preparing MTX-COVAB for clinical evaluation.

• MTX-COVAB is a human-derived antibody that targets SARS-CoV-2.

On May 20, 2021, RenBio announced that it signed a license agreement with Columbia University, giving **RenBio the exclusive worldwide development and commercialization rights to RB-100** for COVID-19, which was developed in the lab of David D. Ho, M.D. of Columbia University. In preclinical studies, RB-100 demonstrated robust antiviral activity against SARS-CoV-2 variants that have recently emerged from the U.K. (B.1.1.7), South Africa (B.1.351), Brazil (P.1), California (B.1.427 and B.1.429), and New York City (B.1.526). RenBio is expected to complete IND-enabling preclinical studies and initiate a Phase 1/2 clinical trial of RB-100 in 2021.

 RB-100 is a bispecific antibody that targets two distinct sites on the spike of SARS-CoV-2.

On May 27, 2021, Zydus Cadila announced that they are seeking **permission to initiate Phase 1/3 clinical trials of ZRC-3308** from the Drugs Controller General of India.

 ZRC-3308 is a cocktail of two SARS-CoV-2-neutralizing monoclonal antibodies that are designed to have a long half-life providing protection for a long period of time and reduced immune-effector functions to minimize potential tissue damaging side effects of virus neutralizing monoclonal antibodies.

First Phase 2 studies of COVI-DROPS to start

On May 25 and 28, 2021, details were posted on clinicaltrials.gov for Phase 2 studies to evaluate the efficacy, safety and pharmacokinetics of a single intranasal dose of STI-2099 (COVI-DROPS[™]) in outpatient adults with COVID-19. Sponsored by Sorrento Therapeutics, Inc., the studies have an estimated enrollment of 72 patients in the US (NCT04906694) and 350 in the UK (NCT04900428). Due to start in August and July 2021 in the US and UK, respectively, the studies have estimated primary completion dates in December 2021 and January 2022, respectively.

• COVI-DROPS is a human monoclonal antibody that targets SARS-CoV-2.

Phase 3 study of BI 767551 to post-exposure prevention to start

On May 25, 2021, details were posted on clinicaltrials.gov for a Phase 2/3 randomized,

double-blind, placebo-controlled, parallel-group, group-sequential study (NCT04894474) to evaluate efficacy, safety and tolerability of BI 767551 for post-exposure prevention of SARS-CoV-2 infection in household contacts to a confirmed SARS-CoV-2 infected individual. BI 767551 will be administered via inhalation and intravenous infusion. Sponsored by Boehringer Ingelheim, the study has an estimated enrollment of 1700 patients. Due to start in June 2021, the study has an estimated primary completion date in May 2022.

• BI 767551 is a human monoclonal antibody that targets SARS-CoV-2.

EUA requested for lenzilumab

On May 28, 2021, Humanigen announced that the company submitted an application to the U.S. Food and Drug Administration (FDA) for Emergency Use Authorization (EUA) for lenzilumab in COVID-19. Positive clinical study results were obtained from the LIVE-AIR Phase 3 study evaluating the ability of lenzilumab to improve the likelihood of survival without ventilation in newly hospitalized COVID-19 patients.

• Lenzilumab is a human IgG1 antibody targeting GM-CSF.

FDA issues statement on leronlimab for COVID-19

On May 17, 2021, FDA issued a statement indicating that the **clinical data currently available do not support the clinical benefit of leronlimab for the treatment of COVID-19**. Their statement was based on results currently available for two separate clinical trials investigating leronlimab for the treatment of COVID-19 that were conducted by CytoDyn. Study CD10, which included 86 patients, studied leronlimab's effect on mildto-moderate COVID-19 disease. Study CD12, which included 394 patients, studied leronlimab's effect on severe symptoms of respiratory illness associated with COVID-19. Primary and secondary endpoints were not met in either study.

 Leronlimab, a humanized IgG4 antibody, targets CCR5, which is a G proteincoupled receptor that regulates trafficking and effector functions of memory/effector T-lymphocytes, macrophages, and immature dendritic cells.

Sotrovimab receives FDA's emergency use authorization for COVID-19

On March 27, 2021, the **FDA issued an EUA for sotrovimab** (VIR-7831; GSK4182136) for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progression to severe COVID-19, including hospitalization or death. The EUA was issued to GlaxoSmithKline.

Sotrovimab, a human anti-SARS-CoV2 antibody, is being evaluated in a Phase 1/2/3 randomized, double-blind, placebo-controlled clinical trial in non-hospitalized adults with mild-to-moderate COVID-19 symptoms and a positive SARS-CoV-2 test result. The EUA is based on an interim analysis of results for 583 patients in the study, 291 and 292 of whom received sotrovimab or placebo, respectively, within five days of onset of COVID-19 symptoms. The primary endpoint was progression of COVID-19 (defined as hospitalization for greater than 24 hours for acute management of any illness or death from any cause) through day 29. Hospitalization or death occurred in 21 (7%) patients who received placebo compared to 3 (1%) patients treated with sotrovimab.

Updates on non-COVID-19 interventions

First-in-human studies due to start soon

On May 20, 2021, details were posted on clinicaltrials.gov for a Phase 1/2 study (**NCT04895709**) of BMS-986340 as monotherapy and in combination with nivolumab in participants with advanced solid tumors. Sponsored by Bristol-Myers Squibb, the study has an estimated enrollment of 185 patients. Due to start in late May 2021, the study has an estimated primary completion date in March 2024.

• BMS-986340 is an anti-CCR8 hlgG1-nonfucosylated antibody.

On May 21, 2021, details were posted on clinicaltrials.gov for a first-in-human, multicenter, Phase 1/2, open-label study (**NCT04896697**) of XTX101 in patients with advanced solid tumors. Sponsored by Xilio Development, Inc., the study has an estimated enrollment of 72 patients. Due to start in August 2021, the study has an estimated primary completion date in March 2026.

• XTX101 is an Fc-engineered anti-CTLA4 monoclonal antibody.

On May 24, 2021, details were posted on clinicaltrials.gov for a Phase 1 study (**NCT04898634**) of JNJ-78278343 for advanced prostate cancer. Sponsored by Janssen Research & Development, LLC, the study has an estimated enrollment of 70 patients. Due to start in July 2021, the study has an estimated primary completion date in May 2023.

• JNJ-78278343 is a humanized IgG1-based bispecific antibody designed to direct T cells to human kallikrein 2-positive target tumor cells.

On May 27, 2021, details were posted on clinicaltrials.gov for a Phase 1/2 study (**NCT04903873**) to evaluate safety, efficacy, and pharmacokinetics of EU101 in patients with advanced solid tumors. Sponsored by Eutilex, the study has an estimated enrollment of 96 patients. Due to start in late May 2021, the study has an estimated primary completion date in September 2023.

• EU101 is an agonistic anti-CD137 (4-1BB) monoclonal antibody.

Biogen to start Phase 3 study of BIIB059

On May 20, 2021, details were posted on clinicaltrials.gov for a Phase 3 study (**NCT04895241**) to evaluate the efficacy and safety of BIIB059 in adult participants with active systemic lupus erythematosus receiving background nonbiologic lupus standard of care. Sponsored by Biogen, the study has an estimated enrollment of 540 patients. Due to start in June 2021, the study has an estimated primary completion date in April 2025.

• **BIIB059 is a humanized IgG1** antibody that targets blood dendritic cell antigen 2 (BDCA2), which is uniquely expressed on the surface of human plasmacytoid DCs.

Fast Track designation granted for apitegromab

On May 24, 2021, Scholar Rock announced that the **FDA granted Fast Track designation for apitegromab** for the treatment of patients with spinal muscular atrophy (SMA). FDA previously granted Orphan Drug and Rare Pediatric Disease designations, and the European Medicines Agency has granted Priority Medicines (PRIME) designation and Orphan Medicinal Product designation, to apitegromab for the treatment of SMA. The company anticipates initiating a Phase 3 trial of apitegromab in patients with nonambulatory Type 2 and 3 SMA by the end of 2021.

• Apitegromab is a human IgG4 lambda monoclonal antibody that targets promyostatin.

BLAs for anti-PD-1 sintilimab and penpulimab submitted

On May 18, 2021, Innovent Biologics, Inc. and Eli Lilly and Company jointly announced that the **FDA accepted for review a BLA for sintilimab** injection in combination with pemetrexed and platinum chemotherapy for the first-line treatment of people with nonsquamous non-small cell lung cancer (NSCLC). This regulatory application was primarily based on the results of the Phase 3 ORIENT-11 trial. FDA's deadline for a first action on sintilimab application is in March 2022.

• Sintilimab is a human IgG4 antibody that targets PD-1.

On May 24, 2021, Akeso, Inc. announced that a **BLA had been submitted to FDA for penpulimab** for third-line treatment of metastatic nasopharyngeal carcinoma. The FDA will review the BLA under the Real-Time Oncology Review program, which aims to accelerate the process of drug approval. Penpulimab had previously been granted Breakthrough Therapy and Fast Track designations from the FDA for this disease.

• Penpulimab is a humanized IgG1 mAb that targets PD-1. The antibody was engineered to eliminate Fc-mediated effector function, and to slow the off-rate on antigen binding, resulting in improved receptor occupancy.

FDA advisory committee votes in favor of teplizumab

On May 27, 2021, the majority of **FDA's Endocrinologic and Metabolic Drugs Advisory Committee members voted in favor of teplizumab.** The Advisory Committee voted 10 yes and 7 no on the question, "Does the information provided in the background documents and presentations by the Applicant and FDA show that the benefits of teplizumab outweigh the risks in support of approval to delay clinical type 1 diabetes mellitus?". FDA's deadline for an action on the application is July 2, 2021.

• Teplizumab, also called hOKT31(Ala-Ala), is a humanized, non-Fc receptor binding, anti-CD3 monoclonal antibody.

FDA extends review of narsoplimab

On May 20, 2021, Omeros Corporation reported that the **FDA will require additional time to review the BLA for narsoplimab** for the treatment of hematopoietic stem cell transplant-associated thrombotic microangiopathy. The new Prescription Drug User Fee Act (PDUFA) target action date is October 17, 2021.

• Narsoplimab is a human IgG4 lambda monoclonal antibody targeting mannanbinding lectin-associated serine protease-2.

FDA approves bispecific amivantamab for NSCLC

On May 21, 2021, the **FDA approved Rybrevant (amivantamab-vmjw)** as the first treatment for adult patients with NSCLC whose tumors have specific types of genetic mutations: epidermal growth factor receptor (EGFR) exon 20 insertion mutations. Rybrevant received Priority Review and Breakthrough Therapy designation for this indication. The efficacy of amivantamab was evaluated in a study of 81 patients with NSCLC and EGFR exon 20 insertion mutations whose disease had progressed on or after platinum-based chemotherapy. In the trial population in which all patients received the drug, the overall response rate was 40% and the median duration of response was 11.1 months, with 63% of patients having a duration of response of 6 months or more.

• Amivantamab (JNJ-61186372; Janssen Pharmaceutical Companies of Johnson & Johnson) is a human, low-fucose IgG1-based bispecific antibody targeting EGFR

and mesenchymal epithelial transition factor (MET) that was created using Genmab's DuoBody technology.

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Antibody News You Should Know

June 1 - 15, 2021

Upcoming Webinar

Staying ahead of the virus:

From a multispecies discovery strategy to highly efficacious, clinically suitable multi-antibody cocktails targeting SARS-CoV-2

Presented by: Debby Kruijsen, Ph.D. & Ilse Roodink, Ph.D.

Thursday, June 17th

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COVID-19 intervention news

New anti-SARS-CoV-2 antibodies aim for the clinic

On June 2, 2021, Centivax Inc. announced that it has entered into a strategic partnership with the U.S. Naval Medical Research Center for **Phase 1 clinical development of Centi-B9**, which has been bioengineered for high stability, low viscosity high concentration (250mg/ml) delivery, enabling a prophylactic or therapeutic dose of

Centi-B9 to be delivered in a non-hospital setting through a single injection. The Phase 1 trial will demonstrate safety and pharmacokinetics of Centi-B9 in healthy volunteers and is planned to begin in July 2021.

• Centi-B9 is an antiSARS-CoV-2 broad-spectrum injectable antibody therapeutic and prophylactic.

On June 03, 2021, IGM Biosciences, Inc. announced the **expansion of its IgM antibody platform into infectious diseases**, with the anticipated advancement of a new pipeline candidate, IGM-6268, into the clinic in the third quarter of 2021. The company's new paper 'Nasal delivery of an IgM offers broad protection from SARS-CoV-2 variants', **online at Nature**, describes preclinical data for the engineered IgM antibody named IgM-14, which potently neutralizes the virus, including variants of concern and other receptor-binding domain mutants.

• IGM-6268 is an IgM version of an anti-SARS-CoV-2 IgG monoclonal antibody being developed as an intranasally administered agent for the treatment and prevention of COVID-19.

Results for Phase 3 clinical studies of anti-SARS-CoV-2 antibodies announced

On June 14, 2021, Celltrion Group announced top-line efficacy and safety data from a global Phase III clinical trial, demonstrating that anti-SARS-CoV-2 monoclonal antibody, regdanvimab (CT-P59), met all primary and key secondary endpoints in patients with mild- to- moderate symptoms of COVID-19 (n=1,315). Results showed that CT-P59 significantly reduced the risk of hospitalization or death by 72% for patients at high- risk of progressing to severe COVID-19 up to Day 28, compared to placebo. Regdanvimab was granted conditional use authorization in South Korea.

• Regdanvimab is an anti-SARS-CoV-2 antibody derived from B cells of convalescent patients.

On June 15, 2021, AstraZeneca announced results from the Phase 3 STORM CHASER trial assessing the safety and efficacy of AZD7442, a long-acting antibody combination, for the prevention of symptomatic COVID-19 in participants recently exposed to the SARS-CoV-2 virus. The **trial did not meet the primary endpoint** of post-exposure prevention of symptomatic COVID-19 with AZD7442 compared to placebo.

• AZD7442 is a combination of 2 anti-SARS-CoV-2 antibodies, tixagevimab (AZD8895) and cilgavimab (AZD1061), which were derived from B cells donated by convalescent patients.

Updates on non-COVID-19 interventions

Iksuda Therapeutics secures financing to advance ADC assets

On June 7, 2021, Iksuda Therapeutics announced it has completed a US \$47 million financing round, co-led by Mirae Asset Capital and its subsidiaries, Celltrion and Premier Partners. **The funding will support the advancement of Iksuda's lead ADC assets**, including IKS03, and expansion of its payload and conjugation platform technologies. The investment will enable progression of IKS03 to first-in-human Phase 1 clinical trials.

• IKS03 is a CD19-targeted antibody-drug conjugate (ADC) candidate for B-cell cancers.

iTeos Therapeutics and GlaxoSmithKline plc partner to advance EOS-448

On June 14, 2021, **iTeos Therapeutics and GlaxoSmithKline plc announced an agreement to co-develop and co-commercialize EOS-448**, which is currently being evaluated in a Phase 1 development clinical study as a potential treatment for patients with cancer. GSK and iTeos plan to start combination studies of EOS-448 with dostarlimab in 2022.

• EOS-448 is an anti-TIGIT monoclonal antibody.

First-in-human studies to start soon

On June 07, 2021, Cullinan Oncology, Inc. announced that the FDA has cleared Cullinan Florentine's IND application for CLN-049 for the treatment of relapsed/refractory acute myeloid leukemia. In preclinical studies, CLN-049 led to potent FLT3-dependent killing of leukemic cells in vitro at a wide range of FLT3 expression levels on AML cells. Treatment with CLN-049 led to survival benefit in an AML xenograft model and complete elimination of leukemic blasts in various mouse models implanted with primary patient leukemic cells or AML cell lines.

• CLN-049 is a bispecific antibody targeting FLT3 and CD3.

On June 3, 2021, details were posted in clinicaltrials.gov for two Phase 1 studies of IBI321. Sponsored by Innovent Biologics (Suzhou) Co. Ltd , the NCT04911894 and NCT04911881 studies will evaluate the safety,

tolerability and primary efficacy of IBI321 in patients with advanced solid tumors. These studies are not yet recruiting patients. Due to start in June 2021, both studies have primary completion dates in January 2023.

• IBI321 is a bispecific antibody that targets PD-1 and TIGIT.

On June 4, 2021, details were posted in clinicaltrials.gov for a Phase 1, first-in-human study (**NCT04914117**) of RC118 for patients with locally advanced unresectable/metastatic solid tumors, which is due to start in August 2021. Sponsored by RemeGen Co., Ltd., the study's estimated enrollment is 33 patients.

• RC118 is an ADC targeting an undisclosed antigen.

On June 10, 2021, CASI Pharmaceuticals, Inc. announced First-Patient-In in the **Phase 1 dose escalation and expansion study of CID-103** in patients with previously treated, relapsed or refractory multiple myeloma. CASI licensed the global rights to CID-103 from Tusk Therapeutics, Ltd in April 2019

• CID-103 is a human IgG1 monoclonal antibody that recognizes a unique epitope on CD38.

Phase 2 study of VIB7734 started

On June 14, 2021, details were posted in clinicaltrials.gov for a Phase 2 efficacy and safety study (**NCT04925934**) of VIB7734 for the treatment of moderate to severely active systemic lupus erythematosus. Sponsored by Viela Bio, the study is recruiting an estimated 195 participants and has a primary completion date in July 2023.

• VIB7734, also known as MEDI7734 and daxdilimab, is a human IgG1 antibody that targets ILT7 on plasmacytoid dendritic cells.

Phase 3 study of BD0801 to start soon

On June 1, 2021, details were posted in clinicaltrials.gov for a Phase 3 study (**NCT04908787**) of BD0801 injection combined with chemotherapy versus placebo combined with chemotherapy in patients with recurrent, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer. Sponsored by Jiangsu Simcere Pharmaceutical Co., Ltd., the study will recruit and estimated 357 patients and has a primary completion date in December 2023.

• BD0801, also known as APX003 and sevacizumab, is a humanized antibody targeting VEGF.

Teclistamab granted FDA's Breakthrough Therapy designation for multiple myeloma

On June 1, 2021, The Janssen Pharmaceutical Companies of Johnson & Johnson announced that the U.S. Food and Drug Administration (FDA) has granted **Breakthrough Therapy Designation for a bispecific antibody**, **teclistamab**, in the treatment of relapsed or refractory multiple myeloma. Teclistamab received a PRIME (PRIority MEdicines) designation from the European Medicines Agency earlier this year. It is currently being evaluated in a Phase 2 clinical study for the treatment of relapsed or refractory multiple myeloma.

• Teclistamab is humanized DuoBody® Antibody that targets B-cell maturation antigen and CD3.

Disitamab vedotin approved in China

On June 9, 2021, the **approval in China of anti-HER2 ADC disitamab vedotin** (also known as vedicitumumab; trade name: Aidixi®, research code: RC48) for the treatment of patients with locally advanced or metastatic gastric cancer (including gastroesophageal junction adenocarcinoma) who have received at least 2 types of systemic chemotherapy was announced.

• Disitamab vedotin is a humanized anti-HER2 IgG1 kappa antibody conjugated to MMAE, a cytotoxic drug.

FDA approves Aduhelm (aducanumab)

On June 7, 2021, the **FDA approved Aduhelm (aducanumab)** for the treatment of Alzheimer's disease. The late-stage development program for Aduhelm consisted of two Phase 3 clinical trials. One study met the primary endpoint, showing reduction in clinical decline. The second trial did not meet the primary endpoint. In all studies in which it was evaluated, Aduhelm reduced the level of amyloid plaques in the brain in a dose- and time-dependent fashion. The reduction in amyloid plaque is considered a surrogate for a reduction in clinical decline. Aduhelm was approved using FDA's accelerated approval pathway, which can be based on the drug's effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients. A post-approval trial to verify that the drug provides the expected clinical benefit is required.

Biogen licensed the worldwide rights to aducanumab from Neurimmune in 2007, and has collaborated with Eisai on the global development and commercialization of aducanumab since 2017.

• Aducanumab is a human IgG1 antibody that targets anti-amyloid beta.

Antibody News You Should Know

June 15 - July 1, 2021

Please join us for the next webinar in our Antibody Discovery & Development series!



Antibody Fc Engineering: Designing Antibodies for Cancer, Covid-19, and Beyond

Speaker: Alicia Chenoweth, PhD, King's College London

Date/time: Thursday July 8, 2021 at 8am PT/11am ET/5pm CET

Click here to register for this free event

COVID-19 intervention news

Phase 2 study of LY-CovMab planned

On June 15, 2021, **Luye Pharma Group announced** that its subsidiary Boan Biotech submitted an application to the US Food and Drug Administration (FDA) to start a Phase 2 study evaluating the efficacy, safety, tolerability, pharmacokinetics and immunogenicity of LY-CovMab injection in patients with mild to moderate COVID-19. Trial sites will be located in the US, Europe and China. LY-CovMab was developed using Shandong Boan's full-human antibody transgenic mouse technology and phage display technology.

 LY-CovMab is a human monoclonal neutralizing antibody that specifically binds to the SARS-CoV-2 surface spike protein receptor binding domain with high affinity.

Emergency Use Authorization granted for tocilizumab for COVID-19 On June 24, 2021, the FDA issued an Emergency Use Authorization (EUA) for intravenous Actemra® (tocilizumab) for the treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation. The EUA was issued to Genentech Inc.

 Actemra is a recombinant humanized monoclonal antibody that inhibits inflammation by selectively binding to both soluble and membrane-bound human IL-6 receptors and subsequently inhibiting IL6-mediated signaling through these receptors.

Updates on non-COVID-19 interventions

Breakthrough Therapy designations for investigational Alzheimer's disease therapies

On June 24, 2021, Eli Lilly and Company announced **FDA granted Breakthrough Therapy designation for donanemab for Alzheimer's disease**. Lilly intends to submit a biologics license application for donanemab under the accelerated approval pathway later this year based on data from the Phase 2 TRAILBLAZER-ALZ study (**NCT03367403**) of patients with early symptomatic Alzheimer's disease.

• Donanemab is a humanized IgG1 antibody targeting amyloid beta.

On June 24, 2021, Eisai Co., Ltd. and Biogen Inc. announced that the **FDA granted Breakthrough Therapy designation for lecanemab (BAN2401) for the treatment of Alzheimer's disease**. Lecanemab is undergoing evaluation in Phase 3 clinical studies of patients with the disease.

• Lecanemab is a humanized IgG1 anti-amyloid beta protofibril antibody.

First Phase 3 studies of 5 mAbs pending or underway

On June 15 and 23, 2021, details were posted on clinicaltrials.gov for Phase 3 studies of inclacumab. The **NCT04927247** study will assess the ability of a single dose of inclacumab to reduce re-admission in participants with sickle cell disease and recurrent vaso-occlusive crises. Inclacumab (30 mg/kg) will be administered intravenously and the effects will be compared to placebo. In the **NCT04935879** study, the safety and efficacy of inclacumab in participants with sickle cell disease experiencing vaso-occlusive crises will be assessed. Sponsored by Global Blood Therapeutics, the study estimated start dates are July 1 and June 30, 2021.

 Inclacumab is a human IgG4 antibody that targets CD62, an antigen also known as P-selectin. Global Blood Therapeutics acquired rights to inclacumab from Roche Holding in 2018. On June 16, 2021, details were posted on clinicaltrials.gov for a Phase 3 study (**NCT04928846**) of telisotuzumab vedotin (ABBV-399) versus docetaxel in subjects with previously treated c-Met+, EGFR wildtype, locally advanced/metastatic non-squamous non-small cell lung cancer. Sponsored by AbbVie, an estimated 600 patients will participate in the study, which has an estimated start date of December 10, 2021.

• Telisotuzumab vedotin is a humanized IgG1 antibody cMet (also known as hepatocyte growth factor receptor) conjugated to MMAE.

On June 23, 2021, details were posted on clinicaltrials.gov for a Phase 3 study (**NCT04935359**) of the efficacy and safety of NIS793 in combination with standard of care chemotherapy in first-line metastatic pancreatic ductal adenocarcinoma. Sponsored by Novartis, an estimated 490 patients will participate in the study, which has an estimated start date of October 13, 2021.

 NIS793 is a human, high-affinity monoclonal antibody that neutralizes TGFβ1 and 2 while sparing TGFβ3

On June 17, 2021, BeiGene, Ltd. announced that the first patient was dosed in the global **Phase 3 AdvanTIG-302 trial of BeiGene's investigational antibody ociperlimab** (BGB-A1217) in combination with its anti-PD-1 antibody tislelizumab, for the first-line treatment of patients with locally advanced, unresectable, or metastatic non-small cell lung cancer whose tumors exhibit high PD-L1 expression and do not harbor EGFR-sensitizing mutations or ALK translocations.

• Ociperlimab is a humanized IgG1 antibody that targets TIGIT.

On June 17, 2021, Biogen Inc. announced that the first patient has been dosed in the global **Phase 3 clinical study**, **TOPAZ-1**. The study will evaluate the clinical efficacy and assess the safety of BIIB059, as compared to placebo, in participants with active systemic lupus erythematosus. Participants will be randomized to receive subcutaneous treatment with BIIB059 at one of two doses or placebo every four weeks with an additional dose at Week 2, in addition to their existing lupus therapy.

 BIIB059 is a humanized IgG1 mAb that specifically recognizes blood dendritic cell antigen 2, which is uniquely expressed on the surface of human plasmacytoid dendritic cells.

Tralokinumab granted marketing authorization in EU

On June 17, 2021, the European Commission approved Adtralza® (tralokinumab) for the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy. The European Commission decision is valid in all European Union Member States, Iceland, Norway, and Liechtenstein. Originally identified by Cambridge Antibody Technology and developed by MedImmune as CAT-354, AstraZeneca sold the rights to tralokinumab in dermatology indications to LEO Pharma in 2016. A biologics license application (BLA) for tralokinumab for atopic dermatitis is undergoing review in the US; the first action on the BLA is expected in the second quarter of 2021.

 Tralokinumab is a human IgG4I antibody targeting IL-13, a pleiotropic T helper type 2 cytokine associated with atopic dermatitis and other inflammatory disorders. The antibody interferes with IL-13-mediated signaling by blocking its interactions with both IL-13 receptor α1 and IL-13 receptor α2.

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