Antibody News You Should Know

July 1 - 15, 2020

Updates on non-COVID-19 interventions

Marketing application news

On July 6, 2020, Daiichi Sankyo Company, Limited announced that the European Medicines Agency (EMA) has validated the Marketing Authorization Application for trastuzumab deruxtecan for the treatment of adults with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens. Trastuzumab deruxtecan was granted accelerated assessment by the EMA's Committee for Medicinal Products for Human Use. The US Food and Drug Administration (FDA) granted accelerated approval to fam-trastuzumab deruxtecan-nxki (ENHERTU®) in December 2019.

• Trastuzumab deruxtecan is an antibody-drug conjugate that targets the human epidermal growth factor receptor 2 (HER2).

On July 8, 2020, Biogen and Eisai Co., Ltd. announced that **Biogen has completed the submission of a Biologics License Application (BLA) to the FDA for the approval of aducanumab** for Alzheimer's disease. The FDA has up to 60 days to decide whether to accept the application for review.

• Aducanumab is a human IgG1 targeting amyloid beta licensed by Biogen from Neurimmune.

On July 9, 2020, **LEO Pharma announced that the FDA has accepted the BLA for tralokinumab** for the treatment of adults with moderate-to-severe atopic dermatitis. FDA's target action date has been set in the second quarter of 2021. EMA recently accepted the marketing authorization application for tralokinumab. • Tralokinumab is a human IgG4 monoclonal antibody that targets interleukin-13.

On July 13, 2020, **CytoDyn Inc. announced it received a Refusal to File letter from the FDA regarding its BLA for leronlimab** as a combination therapy with HAART for highly treatment experienced HIV patients. The FDA requested additional analysis of completed trials, but no additional clinical trials are required.

 Leronlimab (PRO140) is a humanized IgG4 monoclonal antibody targeting CCR5, a cellular receptor that is relevant in HIV infection, tumor metastases, and other diseases.



COVID-19 intervention news

Anti-SARS-CoV-2 antibodies

On July 15, 2020, IDBiologics indicated that they plan to file an Investigational New Drug (IND) application and **start human testing of IDB003**, an **anti-SARS-CoV-2 monoclonal antibody**, in the third quarter of 2020. IDBiologics licensed IDB003, identified in Dr. James Crowe's lab at the Vanderbilt Vaccine Center, and is developing it to treat SARS-CoV-2 infections.

On July 12, 2020, Junshi Biosciences announced the completion of study

subjects enrollment in a Phase 1 trial of anti-SARS-CoV-2 monoclonal antibody JS016. The company plans to initiate a Phase 1b trial in non-severe COVID-19 patients and Phase 2/3 trials in severe and critical patients soon, and they will investigate the prophylactic potential of JS016 in high-risk population.

 JS016 targets the SARS-CoV-2 spike protein receptor-binding domain (RBD) and can effectively block the binding of viruses to host cell surface receptor ACE2.

On July 6, 2020, **Regeneron Pharmaceuticals, Inc. announced the initiation of late-stage clinical trials evaluating REGN-COV2**. A Phase 3 trial will evaluate REGN-COV2's ability to prevent infection among uninfected people who have had close exposure to a COVID-19 patient, and is being run jointly with the National Institute of Allergy and Infectious Diseases. REGN-COV2 has also moved into the Phase 2/3 portion of two adaptive Phase 1/2/3 trials testing its ability to treat hospitalized and non-hospitalized patients with COVID-19.

 REGN-COV2 (REGN10933+REGN10987) is a cocktail of 2 monoclonal antibodies derived from discovery efforts using both humanized VelocImmune® mice and blood samples from recovered COVID-19 patients. The antibodies target multiple different regions of the RBD of the SARS-CoV-2 spike protein.

Antibodies targeting non-viral antigens

On July 6, 2020, CSL Behring announced that the **first patient has been enrolled in its Phase 2 study (NCT04409509) to assess the safety and efficacy of CSL312** to treat patients suffering from severe respiratory distress. Estimated enrollment in the study is 124 patients, and the estimated primary completion date is in December 2020.

• CSL312 (garadacimab) is a human IgG4 Factor XIIa antagonist monoclonal antibody.

On July 7, 2020, Corvus Pharmaceuticals, Inc. announced that it **initiated a Phase 1 study (NCT04464395) to investigate a CPI-006** as therapy for patients with COVID-19. The study is expected to enroll up to 30 patients at several sites in the United States, and has a primary completion date in March 2021.

• CPI-006 is a humanized anti-CD73 antibody that may increase COVID-19 antibody production via B cell activation, and thereby reduce the severity and duration of infection.

On July 2, 2020, Regeneron Pharmaceuticals, Inc. and Sanofi announced that the U.S. Phase 3 trial of Kevzara® (sarilumab) 400 mg in COVID-19 patients requiring mechanical ventilation did not meet its primary and key secondary endpoints when Kevzara was added to best supportive care compared to best supportive care alone. Based on the results, the U.S.-based trial has been stopped, including in a second cohort of patients who received a higher dose of Kevzara (800 mg).

• Sarilumab is a human monoclonal antibody targeting the interleukin-6 receptor. It is approved for the treatment of rheumatoid arthritis.

On July 11, 2020, Biocon Limited announced that the Drugs Controller General of India approved itolizumab for emergency use in India for the treatment of cytokine release syndrome in moderate to severe acute respiratory distress syndrome due to COVID-19.

 Itolizumab is a humanized anti-CD6 monoclonal antibody developed by Biocon Biologics that was previously approved in India for chronic plaque psoriasis. Its mechanism of action involves blocking the activation of T lymphocytes, thereby suppressing production of pro-inflammatory cytokines.

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Clinical studies started

On July 21, 2020, **Staten Biotechnology B.V. announced the initiation of dosing of STT-5058** in a first-in-human clinical study. The Phase 1 NCT04419688 study will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of single and multiple-ascending doses of intravenously administered STT-5058 in otherwise healthy subjects with elevated triglyceride levels and patient volunteers with moderate hypertriglyceridemia and single-ascending doses of subcutaneously administered STT-5058 in otherwise healthy subjects with elevated triglyceride levels. STT-5058 was licensed from Staten's research collaboration partner argenx and is developed in collaboration with Novo Nordisk.

• STT-5058 is a humanized, monoclonal antibody targeting novel and unique epitopes on apoC3. The antibody has an extended half-life and recycling properties that are pH-dependent.

On July 21, 2020, **Dragonfly Therapeutics**, **Inc. announced it has dosed its first patient in a Phase 1/2 study of DF6002**, a proprietary IL-12 investigational immunotherapy. NCT04423029 is a first-in-human, multiple-ascending dose study that will investigate the safety, tolerability, pharmacokinetics, biological, and clinical activity of DF6002 as a monotherapy and in combination with pembrolizumab in patients with locally advanced or metastatic solid tumors, and expansion in selected indications. • DF6002 is a monovalent human interleukin-12-Fc fusion protein that binds to the IL-12 receptor.

Details for a Phase 1 single and multiple ascending dose study of ADX-914 in healthy adult volunteers sponsored by Q32 Bio Inc. were posted on clinicaltrials.gov on July 24, 2020. The estimated start date of the **NCT04485481** study is September 5, 2020, and the estimated enrollment is 72 participants.

• ADX-914 (formerly known as BMS-986265) is a human anti-IL-7R antibody licensed from Bristol Myers Squibb

On July 27, 2020, **NGM Biopharmaceuticals announced it has initiated the Phase 2 CATALINA study**, a multicenter, randomized, double-masked, shamcontrolled clinical trial to evaluate the safety and efficacy of intravitreal injections of NGM621 in patients with geographic atrophy secondary to age-related macular degeneration.

• NGM621 is a humanized IgG1 monoclonal antibody engineered to potently inhibit activity of complement C3.

Marketing application news

On July 23, 2020, ElsaLys Biotech announced the U.S. Food and Drug Administration (FDA) agreement to start the LEUKOTAC® (inolimomab) submission process for a biologics license application (BLA) for the treatment of steroid-refractory acute graft-versus-host disease, grade II-IV adult patients. The BLA will be reviewed under the FDA's Real-Time Oncology Review pilot program, which aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality by the FDA.

• Inolimomab is a murine IgG1 antibody targeting CD25.

On July 27, 2020, during UCB's 2020 Half Year Financial Results video webcast, the company disclosed that a BLA and a marketing authorization application for bimekizumab for treatment of psoriasis had been submitted to FDA and the European Medicines Agency, respectively, earlier in July. In the webcast, disclosure of the marketing application submissions is at 13.00-13.40 min. In June 2020, UCB announced that bimekizumab Phase 3 data demonstrated superior skin clearance over placebo and Stelara® at Week 16 in adults with moderate-to-severe plaque psoriasis.

• Bimekizumab is a humanized IgG1 targeting IL-17A and F.

On July 29, 2020, **Ridgeback Biotherapeutics LP announced FDA has accepted the BLA and granted priority review designation for Ridgeback's investigational Ebola treatment, ansuvimab** (mAb114). The FDA granted Breakthrough Therapy Designation status to ansuvimab as a treatment for Ebola in September 2019.

 Ansuvimab is a human IgG1 antibody that binds to a highly conserved region of amino acids in the receptor-binding domain of Ebola virus variants and prevents the interaction of the glycoprotein with the NPC1 receptor, thus blocking virus entry into the cytoplasm of the host cell.

FDA grants first approval to tafasitamab-cxix

On July 31, 2020, the **FDA approved Monjuvi® (tafasitamab-cxix)** in combination with lenalidomide for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant. Monjuvi® was approved under accelerated approval by the FDA based on overall response rate. A marketing application for tafasitamab is undergoing evaluation by the EMA.

• Tafasitamab-cxix a humanized Fc-modified cytolytic CD19 targeting monoclonal antibody.

In other news

On July 27, 2020, **Merus N.V. announced that FDA has granted Orphan Drug Designation to zenocutuzumab** (MCLA-128) for the treatment of patients with pancreatic cancer. A Phase 1/2 clinical trial (eNRGy) evaluating zenocutuzumab (MCLA-128) in cancer patients who have solid tumors, including non-small cell lung and pancreatic cancers, that have a neuregulin fusion.

 Zenocutuzumab is an IgG1 bispecific antibody that targets human epidermal growth factor receptor 2 (HER2) and HER3, thereby blocking the interaction of HER3 with its ligand, neuregulin.



COVID-19 intervention news

Anti-SARS-CoV-2 antibodies enter clinical studies

On July 12 and July 13, 2020, Brii Biosciences started Phase 1 clinical studies of

anti-SARS-CoV-2 antibodies BRII-196 (NCT04479631) and BRII-198 (NCT04479644). These randomized, single-blind, placebo-controlled, single ascending dose escalation studies will assess the safety, tolerability, and pharmacokinetics of the antibodies administered intravenously to healthy adult volunteers. The estimated primary completion date of the studies is March 2021.

BRII-196 and BRII-198 are human monoclonal antibodies derived from B
 cells from convalescent patients

On July 17, 2020, **Celltrion Group announced the start of a Phase 1 clinical study of anti-SARS-CoV-2 antibody CT-P59**. The study aims to enroll 32 healthy volunteers to evaluate the safety of the antibody. The trial's completion is expected by Q3 of this year. Celltrion is planning global Phase 2/3 trials in patients with mild and moderate COVID-19 and anticipates promising preliminary results from pivotal studies by the end of the year.

 CT-P59 is a human monoclonal antibody targeting the spike protein of SARS-CoV-2

On July 24, 2020, Sinocelltech Ltd. started a Phase 1 study of anti-SARS-CoV-2 antibody SCTA01. **NCT04483375** is a first-in-human, randomized, double-blinded, placebo-controlled, single ascending dose study of SCTA01 in healthy Chinese subjects. The estimated primary completion date of the study is November 2020.

• SCTA01 is a humanized monoclonal antibody.

In other COVID-19-related news

On July 16, 2020, Adimab, LLC, announced that it has launched Adagio Therapeutics Inc. Adimab developed and optimized antibodies that are broadly protective against SARS-CoV-2, SARS-CoV-1 and two additional circulating bat coronaviruses. All coronavirus-related Adimab assets have been transferred to Adagio Therapeutics Inc., which will focus on developing these molecules into effective therapeutic and prophylactic treatments.

On July 20, 2020, South Korea-based Genexine announced that they will cooperate with Y-Biologics in the development of an antibody candidate discovered by Y-Biologics. The two companies will jointly pay for the development of antibody treatments and share intellectual property rights, with Genexine responsible for the commercialization of products and technologies. Y-Biologics' anti-SARS-CoV-2 antibody candidates were derived from B cells from convalescent patients and their Ymax-ABL human antibody library.

On July 29, 2020, GlaxoSmithKline indicated in their 2020 Q2 results that a study of **VIR-7831 / VIR-7832 (GSK4182136) was expected to start in August 2020**. Vir announced in May that their SARS-CoV-2 antibody development candidates, VIR-7831 and VIR-7832, have demonstrated high affinity for the SARS-CoV-2 spike protein and the ability to neutralize SARS-CoV-2 in live-virus cellular assays.



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COVID-19 intervention news

Anti-SARS-CoV-2 antibodies enter clinical studies

On August 11, 2020, **SAB Biotherapeutics announced that the first participant has been dosed in its Phase 1 study** (NCT04468958) evaluating the safety of SAB-185 in healthy volunteers. Estimated enrollment is 28 subjects, and the estimated primary completion date is in September 2020. A Phase 1b study (NCT04469179) in ambulatory subjects with COVID-19 is slated to begin in mid-August.

 SAB-185 is composed of anti-SARS-CoV-2 human polyclonal immunoglobulin G purified from the plasma of immunized transgenic bovines. The animals were immunized initially with a plasmid DNA vaccine that expresses wild-type SARS-CoV-2 spike protein, followed by additional immunizations with a recombinant spike protein from SARS-CoV-2 produced in insect cells.

On August 11, 2020, details were posted for a **first-in-humans dose escalation study of AZD7442 (AZD8895 + AZD1061)**, which will evaluate its safety, tolerability, pharmacokinetics, and the generation of anti-drug antibodies in healthy adults. The study is intended to enable future studies of AZD7442's efficacy in preventing and treating COVID-19. The NCT04507256 study's estimated enrollment is 48 subjects and the estimated start date is August 17, 2020.

 AstraZeneca announced in June 2020 that it had licensed coronavirusneutralizing antibodies from Vanderbilt University and planned to advance a pair of these mAbs into clinical development as a potential combination therapy for the prevention and treatment of COVID-19.

Phase 3 studies of LY3819253 started

On August 2 and 4, 2020, two Phase 3 studies of Eli Lilly and Company's anti-SARS-CoV-2 antibody LY3819253 were started. NIAID and Lilly are collaborators in both studies.

- The NCT04497987 BLAZE-2 Phase 3 trial will evaluate the efficacy and safety of LY3819253 in preventing SARS-CoV-2 infection and COVID-19 in skilled nursing and assisted living facility residents and staff. The estimated primary completion date is in March 2021.
- The NCT04501978 Phase 3 trial will compare the effects of LY3819253 vs. remdesivir vs placebo in 10,000 hospitalized patients. The estimated primary completion date is in July 2021.

Emergency Use Authorization requested for leronlimab

On August 12, 2020, Cytodyn requested that the Food and Drug Administration grant an Emergency Use Authorization for leronlimab for mild to moderate COVID-19 based on data from the Phase 2 CD10 study (NCT04343651). In this study, patients were randomized to receive weekly doses of 700 mg leronlimab or placebo, both of which were administered via subcutaneous injection. **Top-level results of the study** showed that, in patients with Total Clinical Symptom Scores of \geq 4 at baseline (higher scores equate to poorer health state), at Day 3, more subjects treated with leronlimab reported improvement in total clinical symptom score compared to the placebo group (90% on leronlimab arm vs. 71% on placebo).

• Leronlimab is a humanized IgG4 antibody targeting C-C chemokine receptor type 5.

Updates on non-COVID-19 interventions

License agreement signed for emactuzumab

On August 12, 2020, **Celleron Therapeutics announced the signing of a licensing agreement with Roche** providing Celleron exclusive world-wide rights for the clinical development, manufacturing and commercialization of emactuzumab. Emactuzumab therapy has been shown to significantly reduce as colony stimulating factor-1-dependent macrophages in tenosynovial giant cell tumors.

• Emactuzumab is a humanized IgG1 antibody targeting colony stimulating factor-1 receptor.

First in human studies

On August 6, 2020, **IGM Biosciences announced that the FDA has cleared the company to proceed to conduct clinical trials for IGM-8444**. The proposed multicenter, open-label Phase 1 clinical trial will evaluate IGM-8444 intravenously administered as a monotherapy and in combination with chemotherapy in patients with relapsed and/or refractory solid cancers • IGM-8444 is an IgM antibody targeting the Death Receptor 5 protein.

On August 10, 2020, details were posted for a Phase 1 randomized, double-blind, placebo-controlled, two-part single **ascending dose study to assess the safety, tolerability, and pharmacokinetics of REGN5381** in adult humans. The primary objective of the NCT04506645 study is to evaluate the safety and tolerability of single intravenous doses of REGN5381 in healthy normotensive and otherwise healthy hypertensive adults.

• REGN5381 is an agonist of natriuretic peptide receptor 1 developed by Regeneron Pharmaceuticals.

On August 3, 2020, **Innovent Biologics, Inc. announced that the first patient has been successfully dosed in a Phase 1 clinical trial** (CIBI322A101) of IBI322 in China. The Phase 1a/1b clinical study will evaluate IBI322 in the treatment of patients with advanced malignancies who have failed standard therapy.

• IBI322 is a recombinant anti-CD47/PD-L1 bispecific antibody.

On August 11, 2020, **Byondis B.V. (formerly Synthon Biopharmaceuticals B.V.) announced that the first cancer patients have started treatment with its investigational antibody-drug conjugate SYD1875**. The first-in-human dose-escalation and expansion study (NCT04202705) will evaluate the safety, pharmacokinetics and preliminary efficacy of SYD1875 in patients with 5T4-expressing, locally advanced or metastatic solid tumors. Patients are currently being enrolled in three European oncology centers

• SYD1875 is composed of a humanized IgG1 mAb, and a cleavable linkerdrug called valine-citrulline-seco-duocarmycin-hydroxybenzamideazaindole, targeting the 5T4 oncofetal antigen.

Phase 2 study of VLS-101 to start

On August 7, 2020, details were posted for a Phase 2 study (NCT04504916) evaluating the efficacy, safety, pharmacokinetics, immunogenicity, and pharmacodynamics of VLS-101 in patients with metastatic solid tumors. Estimated enrollment of the study is 90 participants and the estimated study start date is October 2020.

 VLS-101 is an antibody-drug conjugate composed of an antibody targeting receptor tyrosine kinase-like orphan receptor 1 on cancer cells coupled with monomethyl auristatin E.

First approvals for BLENREP and Enspryng

On August 5, 2020, **FDA approved approved belantamab mafodotinblmf** (BLENREP) for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent. BLENREP was granted an accelerated approval for this indication based on response rate. Further adequate and well-controlled studies/clinical trials must be done to verify and describe clinical benefit. Belantamab mafodotin-blmf was evaluated in the Phase 2 DREAMM-2 (NCT03525678), an open-label, multicenter trial. Efficacy was based on overall response rate (ORR) and response duration. In patients receiving the recommended dose of 2.5 mg/kg, the ORR was 31% (97.5% CI: 21%, 43%), and 73% of responders had response durations ≥6 months.

 Belantamab mafodotin-blmf is an antibody-drug conjugate composed of a humanized IgG1 antibody targeting B-cell maturation antigen and the cytotoxic agent maleimidocaproyl monomethyl auristatin F.

On August 14, 2020, **Genentech announced that the FDA approved satralizumab-mwge** (Enspryng[™]) as the first and only subcutaneous

treatment for adults with anti-aquaporin-4 (AQP4) antibody positive neuromyelitis optica spectrum disorder (NMOSD). NMOSD is a rare autoimmune disorder of the central nervous system that primarily damages the optic nerve(s) and spinal cord, causing blindness, muscle weakness and paralysis. Enspryng was previously approved in Canada, Japan and Switzerland. Applications are under review with other regulatory agencies, including in the European Union and China.

• Satralizumab is a humanized IgG2 antibody that targets IL-6 receptor.



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COVID-19 intervention news

INDs filed for anti-SARS-CoV-2 antibodies

On August 19, 2020, Sorrento Therapeutics, Inc. announced that it had filed an **investigational new drug application (IND) for COVI-GUARD (STI-1499)** for hospitalized COVID-19 patients that day. The Phase 1 (NCT04454398) study of STI-1499 will evaluate the safety, pharmacokinetics and efficacy of a single dose (10 mg, 30 mg, 100 mg, and 200 mg) of the antibody in hospitalized patients with moderate COVID-19. The company aims to receive an EUA (Emergency Use Authorization) for STI-1499 as early as the end of 2020.

• STI-1499 targets the spike protein of SARS-CoV-2. It was identified via screening of Sorrento's G-Mab library.

On August 26, 2020, HiFiBiO Therapeutics announced the submission of an IND application with the US Food and Drug Administration (FDA) for HFB30132A, a novel anti-SARS-CoV-2 antibody for the treatment of COVID-19 patients. A Phase 1 single intravenous administration ascending dose study will assess the safety, tolerability, and pharmacokinetics of HFB30132A in healthy volunteers.

• HFB30132A targets the spike protein of SARS-CoV-2. It was identified from the B cells of a COVID-19 convalescent patient.

Novel antibodies enter clinical studies

On August 18, 2020, details were posted for a Phase 1, randomized, doubleblind, placebo-controlled, single ascending dose, first-in-human study evaluating the safety, tolerability, and pharmacokinetics of AK119 in healthy subjects. The sponsor is Akesobio Australia Pty Ltd. The **NCT04516564** Phase 1 study, which is not yet recruiting patients as of September 1, has an estimated primary completion date of March 2021.

• AK119 is a humanized monoclonal antibody targeting CD73 that will be evaluated as a treatment for COVID-19

On August 31, 2020, details were posted for a first-in-human, randomized, double-blind, placebo controlled, single dose escalation study to evaluate the safety, tolerability, pharmacokinetics, and immunogenicity of SARS-CoV-2 neutralizing antibody BGB-DXP593 in healthy subjects. The sponsor is BeiGene. The **NCT04532294 Phase 1 study of BGB-DXP593** is not yet recruiting patients as of September 1, and has an estimated primary completion date of October 15, 2020.

 BGB-DXP-593 is a SARS-CoV-2 neutralizing antibody drug candidate identified by high-throughput single-cell RNA and VDJ sequencing of antigen-enriched B cells from over 60 convalescent patients. DXP-593 has exhibited strong neutralization potency in preclinical testing, with an IC50 of 1.2 ng/mL and 15 ng/mL against pseudotyped and authentic SARS-CoV-2, respectively.

On August 31, 2020, details were posted for a **Phase 1 clinical study to** evaluate the safety, tolerability, pharmacokinetic characteristics and immunogenicity of a single dose of MW33 in healthy subjects. The sponsor is Mabwell (Shanghai) Bioscience Co., Ltd. The NCT04533048 study start date was August 7, 2020, and the estimated primary completion date is December 2020.

• MW33 is a recombinant human antibody targeting SARS-CoV-2

Phase 2/3 studies of VIR-7831 started

On August 31, 2020, Vir Biotechnology, Inc. and GlaxoSmithKline plc announced that the **first patient was dosed last week in a Phase 2/3 study with VIR-7831** (also known as GSK4182136), for the early treatment of COVID-19 in patients who are at high risk of hospitalization. Initial results of the study may be available before the end of 2020, with complete results expected in the first quarter of 2021, and potentially early access to the antibody treatment as soon as the first half of 2021.

• VIR-7831 is a human monoclonal antibody that targets the SARS-CoV-2 spike protein.

Sarilumab terminated for COVID-19

On September 1, 2020, Sanofi announced that the global Phase 3 trial investigating intravenously administered Kevzara® (sarilumab) at a dose of 200 mg or 400 mg in severely or critically ill patients hospitalized with COVID-19 did **not meet its primary endpoint and key secondary endpoint when Kevzara was compared to placebo added to usual hospital care**. At this time, Sanofi and Regeneron do not anticipate conducting further clinical studies for Kevzara in COVID-19.

• Sarilumab is a human monoclonal antibody that targets interleukin-6 receptor.

Updates on non-COVID-19 interventions

Preclinical developments

On August 25, 2020, Sutro Biopharma, Inc announced that it achieved a clinical supply milestone under its collaboration and license agreement with the healthcare division of Merck KGaA, Darmstadt, Germany. The milestone was achieved with the **delivery of GMP clinical trial supply for the Phase 1 clinical trial testing of M1231**.

 M1231 is a MUC1- and EGFR-targeting bispecific antibody-drug conjugate (ADC) for the treatment of solid tumors. It relies on the strand-exchange engineered domain (SEED) platform from Merck KGaA, Darmstadt, Germany to generate bispecific antibody-like molecules, and was discovered using Sutro's XpressCF® and XpressCF+™ drug discovery and manufacturing technologies. The ADC includes a proprietary linkerwarhead also discovered by Sutro.

First-in-human studies started

On August 24, 2020, Celldex Therapeutics, Inc. announced that enrollment has opened in its open-label, **Phase 1 NCT04440943 study of CDX-527** in patients with advanced or metastatic solid tumors that have progressed during or after standard of care therapy. The study is expected to enroll up to approximately 90 patients with solid tumors, and has an estimated primary completion date in March 2022.

 CDX-527 is a human bispecific antibody targeting PD-L1 and CD27 to help prime and activate anti-tumor T cell responses through CD27 costimulation, while preventing PD-1 inhibitory signals.

On August 24, 2020, Numab Therapeutics AG announced the **first patient has been dosed with a molecule derived from its ND021 program**. This international, multi-center Phase 1/2 clinical study (NCT04442126) will investigate the safety and tolerability of ascending doses of NM21-1480, the company's clinical lead molecule in the ND021 program, in patients with various forms of solid tumors and establish a recommended dose for continued clinical development.

• NM21-1480 is a trispecific anti-PD-L1/anti-4-1BB/anti-human serum albumin single-chain Fv fusion protein.

Phase 2 study of MAU868 started

On August 17, 2020, **Amplyx Pharmaceuticals announced that the first patient has been dosed in its Phase 2 clinical trial** (NCT04294472) evaluating the efficacy and safety of MAU868 for the treatment of BK viremia in kidney transplant recipients.

 MAU868 is a human monoclonal antibody that potently neutralizes all four major genotypes of BK virus (BKV). BKV-associated nephropathy is a leading cause of kidney allograft loss.

BLENREP approved in the European Union

On August 26, 2020, GlaxoSmithKline plc announced the European Commission granted conditional marketing authorisation for BLENREP

(belantamab mafodotin) as monotherapy for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. BLENREP (belantamab mafodotin-blmf) had previously been granted an accelerated approval by FDA (on August 5, 2020) for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent. BLENREP was granted an accelerated approval for this indication based on response rate. • BLENREP is a humanized anti-B-cell maturation antigen ADC.



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Data for Twist Bioscience anti-SARS-CoV-2 antibodies

On September 2, 2020, Twist Bioscience Corporation announced data demonstrating the potent neutralizing effects of multiple potential therapeutic antibodies against SARS-CoV-2. All antibodies are fully human and are either hIgG1, IgG2, or IgG1 VHH Fc. The in vitro studies involved testing more than 200 well characterized monoclonal antibody and VHH nanobody candidates against live virus and pseudovirus cells. Each antibody was chosen for its high and unbiased binding affinity to either the receptor binding domain of the S1 protein of SARS-CoV-2 or the extracellular domain of ACE2 in human cells.

• Data sets can be found on the Twist website.

Anti-SARS-CoV-2 DARPins to enter clinical study

On September 14, 2020, Molecular Partners AG announced the completion of initial Good Manufacturing Practice manufacturing runs of its tri-specific, antiviral DARPin® candidate for COVID-19, MP0420. First in human studies for MP0420 are anticipated to begin in November 2020. The start of clinical

studies for a second antiviral candidate for COVID-19, MP0423, is anticipated in H1 2021.

VIR-7831 Phase 2/3 study details posted

Details for the Phase 2/3 clinical study of anti-SARS-CoV-2 antibody VIR-7831 were first posted on clinicaltrials.gov on September 10, 2020. **NCT04545060** is a randomized, multi-center, double-blind, placebo-controlled study to assess the safety and efficacy of VIR-7831 for the early treatment of COVID-19 in non-hospitalized patients. Estimated enrollment is 1360 participants and the primary outcome measure is the proportion of participants who have progression of COVID-19 through Day 29. The study's primary completion date is January 2021.

 A summary table of all anti-SARS-CoV-2 monoclonal antibodies currently in clinical studies is located on The Antibody Society website.

Update on leronlimab coming soon

On September 10, 2020, CytoDyn announced that they will hold a **conference call on September 16, 2020 at 4pm ET** to provide an update on their discussions with FDA and the U.K. Medicines & Healthcare product Regulatory Agency for emergency use authorization and Fast Track approval, respectively, for leronlimab as a treatment for COVID-19. They will also discuss CytoDyn's upcoming BLA submission for leronlimab for HIV infection.

• Leronlimab is a humanized IgG4 antibody targeting C-C chemokine receptor type 5.

Updates on non-COVID-19 interventions

Anti-CCR8 mabs in preclinical development

On September 1, 2020, **Gilead Sciences**, **Inc announced an agreement with Jounce Therapeutics**, **Inc.** to exclusively license its JTX-1811 program. JTX-1811 is a monoclonal antibody designed to selectively deplete immunosuppressive tumor-infiltrating T regulatory (TITR) cells. An Investigational New Drug application filing for JTX-1811 is anticipated in the first half of 2021.

• JTX-1811 targets C-C chemokine receptor type 8 (CCR8), which is enriched on TITR cells.

On September 2, 2020, **Harbour BioMed presented its newly discovered novel mAb HBM1022** at the 16th PEGS Boston Summit. The company used a combination of next-generation technologies, including single B Cell technology with advanced phage display and hybridoma platforms to successfully develop the antibody.

• HBM1022 targets CCR8, a G-protein coupled receptor. To date, no mAbs targeting CCR8 have been evaluated in clinical studies.

First-in-human studies to start

On September 7, 2020, details for a first-in-humans dose-escalation clinical study of JNJ-75348780 were first posted on clinicaltrials.gov. The **Phase 1 NCT04540796 study** sponsored by Janssen will include participants with non-Hodgkin lymphoma and chronic lymphocytic leukemia. The estimated enrollment is 120 participants and the estimated start date is November 10, 2020. The total study duration will be up to 2.7 years.

• JNJ-75348780 is a human bispecific antibody targeting CD22 on mature and malignant B-lymphocytes and CD3 on T-lymphocytes.

On September 7, 2020, details for a first-in-humans single and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and immunogenicity of HuL001 in healthy volunteers and patients with multiple sclerosis were first posted on clinicaltrials.gov. Sponsored by HuniLife Biotechnology, Inc., the **Phase 1 NCT04540770 study** will enroll an estimated 24 participants; the estimated start date January 2021.

• HuL001 is an anti-enolase 1 monoclonal antibody.

Partnerships and acquisitions

On September 4, 2020, **AbbVie and I-Mab announced that they signed a broad, global collaboration agreement** for the development and commercialization of lemzoparlimab (also known as TJC4 and TJ011133), which was internally discovered and developed by I-Mab for the treatment of multiple cancers. The two partners have the potential to expand the collaboration to additional transformative therapies. Clinical study results have shown that lemzoparlimab is well tolerated as a single agent at a dose range of up to 30 mg/kg without any priming dose.

• Lemzoparlimab is a human mAb targeting CD47, an immune checkpoint target.

On September 13, 2020, Gilead Sciences, Inc. and Immunomedics announced that the companies have entered into a definitive agreement pursuant to which **Gilead will acquire Immunomedics**. The transaction, which values Immunomedics at approximately \$21 billion, was unanimously approved by both the Gilead and Immunomedics Boards of Directors and is anticipated to close during the fourth quarter of 2020. The agreement will provide Gilead with Trodelvy, which was granted accelerated approval by FDA in April 2020 for the treatment of adult patients with metastatic triple-negative breast cancer who have received at least two prior therapies for metastatic disease.

• Trodelvy (sacituzumab govitecan-hziy) is a Trop-2 targeted antibody-drug conjugate.

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World Bispecific, September 22-24, 2020

• Use code TABS10 for a 10% discount.

Festival of Biologics, November 2-5, 2020

• Use code AntiBody15 for a 15% discount.

8th Antibody Industrial Symposium, Nov. 23-24, 2020

• Use code AbS20 for a 20% discount

Antibody Engineering & Therapeutics, Dec 13-17, 2020

• Use code Antibody15 for a 15% discount

Antibody News You Should Know

September 15 - October 1, 2020



COVID-19 intervention news

Preclinical results for anti-SARS-CoV-2 antibodies

On September 28, 2020, IONTAS and FairJourney Biologics, which combined operations in May 2020, announced the **discovery of potent SARS-CoV-2 neutralizing antibodies** as potential therapeutics for COVID-19. The panel of antibodies block infection at doses as low as 20 pM in pseudoviral assays and 100 pM in live coronavirus assays, surpassing or matching the best antibodies reported.

• IONTAS and FairJourney Biologics are in the process of identifying partners to advance the antibodies into the clinic.

On September 28, 2020, Sorrento Therapeutics, Inc. released preclinical data reporting on COVI-GUARD[™] (STI-1499) and COVI-AMG[™] (STI-2020; Affinity Matured COVI-Guard) neutralizing antibodies targeting SARS-CoV-2 in a **preprint publication**. In preclinical cell-based assays, STI-1499 and STI-2020 at concentrations of 6 µg/ml and 78 ng/ml, respectively, showed 100% in vitro neutralization of SARS-CoV-2.

 A Phase 1 clinical trial (NCT04454398) for STI-1499 in hospitalized COVID-19 patients is pending, and Sorrento intends to submit an IND for STI-2020 as soon as possible.

Early-stage clinical studies of anti-SARS-CoV-2 antibodies

On September 18, 2020, Stanford University started a Phase 1 study (**NCT04567810**) in healthy participants to evaluate the safety, tolerability, and pharmacokinetics of single -ascending and multiple doses of an anti-SARS-CoV-2 chicken egg antibody (IgY).

• The anti-SARS-CoV-2 IgY preparation in liquid is administered intranasally with a dropper at doses of 2-8 mg.

On September 24, 2020, Hengenix Biotech Inc. posted details of a randomized, double-blind, placebo-controlled, dose escalation Phase 1 clinical study (**NCT04561076**) to evaluate safety and pharmacokinetics of HLX70 in healthy adult volunteers. The estimated study start date is December 9, 2020.

 HLX70 is a human antibody that targets the anti-SARS-CoV-2 spike protein.

Clinical data for anti-SARS-CoV-2 antibodies

On September 16, 2020, Eli Lilly and Company announced **data from an interim analysis of the randomized, double-blind, placebo-controlled Phase 2 BLAZE-1 clinical trial** (NCT04427501), showing a reduced rate of hospitalization for patients treated with LY-CoV555, a SARS-CoV-2 neutralizing antibody. The trial enrolled mild-to-moderate recently diagnosed COVID-19 patients across four groups (placebo, 700 mg, 2800 mg, and 7000 mg).

• The prespecified primary endpoint, change from baseline in viral load at day 11, was met at the 2800 mg dose level, but not the others.

- LY-CoV555 had a positive impact on the prespecified endpoint of COVID-19-related hospitalization or ER visit, which occurred in 1.7 percent (5/302) of LY-CoV555 patients, pooled across dose groups, as compared to 6 percent (9/150) of placebo patients.
- The trial is ongoing, testing LY-CoV555 in combination with a second Lilly antibody, LY-CoV016, which binds a different epitope in the SARS-CoV-2 spike region.

On September 29, 2020, Regeneron Pharmaceuticals, Inc. announced the **first data from a descriptive analysis of 275 patients** who participated in a seamless Phase 1/2/3 trial of its investigational antibody cocktail REGN-COV2 (REGN10933 and REGN10987). Patients in the trial were randomized 1:1:1 to receive a one-time infusion of 8 grams of REGN-COV2 (high dose), 2.4 grams of REGN-COV2 (low dose) or placebo.

- Treatment with REGN-COV2 reduced viral load and the time to alleviate symptoms in non-hospitalized patients with COVID-19.
- REGN-COV2 treatment also showed positive trends in reducing medical visits.

Updates on non-COVID-19 interventions

Early-stage bispecific antibodies in the news

On September 14, 2020, Cullinan Oncology, LLC, the German Cancer Research Center and the Eberhard Karls University of Tübingen, Faculty of Medicine (University of Tübingen) announced the **formation of Cullinan Florentine**, a company focused on developing CLN-049, a novel bispecific antibody for the treatment of patients with acute myeloid leukemia. Cullinan Florentine has acquired an exclusive license to develop CLN-049 from the University of Tübingen and the German Cancer Research Center. The company plans to file an investigational new drug (IND) application by the end of the year.

 CLN-049 is a bispecific antibody that binds to the extracellular domain of FLT3 and to CD3.

On September 21, 2020, Light Chain Bioscience announced that it has achieved two milestones and received corresponding payments under its research and collaboration agreement with the LamKap Bio Group, Pfäffikon, Switzerland. The collaboration aims at developing bispecific antibodies capable of re-targeting T cells to tumor cells as well as blocking the immune checkpoint CD47 on the same tumors for the treatment of solid cancers. These milestones were achieved upon the successful completion of the discovery phase and designation by LamKap Bio of bispecific antibodies as clinical development candidates with approval to advance to IND-enabling studies and GMP manufacturing with its partner Lonza, Basel, Switzerland.

- NILK-2301 binds to a tumor-associated antigen (TAA) and CD3 on T-cells, re-targeting T cells to kill tumor cells.
- NILK-2401 is targeted to a TAA and to CD47 on tumor cells, thus causing increased antibody-dependent cellular phagocytosis and antibodydependent cell-mediated cytotoxicity.
- Both NILK-2301 and NILK-2401 can be used as monotherapy and/or in combination.

On September 15, 2020, EpimAb Biotherapeutics announced that the US Food and Drug Administration (FDA) cleared an IND application for EMB-02, a bispecific antibody for cancer based on EpimAb's proprietary FIT-Ig® (Fabs-In-Tandem Immunoglobulin) technology.

• EMB-02 targets two checkpoint proteins, PD-1 and LAG-3.

Details for a Phase 1 study of the T-cell engager RO7293583 were first posted on September 16, 2020. The **NCT04551352 study** will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of RO7293583 in participants with metastatic melanoma. The estimated start date is November 2, 2020; this study is not yet recruiting patients.

• R07293583 is a TYRP1-targeting CD3 T-cell engager.

On October 01, 2020, Teneobio, Inc. and its affiliate TeneoTwo, Inc. announced that their **IND for TNB-486**, a bispecific T-cell engaging antibody for the treatment of B-Cell non-Hodgkin's lymphoma was cleared for the initiation of Phase I clinical studies by the FDA.

• TNB-486 is a human bispecific antibody that binds CD19 and CD3.

Clinical study of anti-CD117 antibody started

On September 22, 2020, Jasper Therapeutics, Inc. announced that the first patient has been dosed in a multicenter **Phase 1 clinical trial of JSP191**. The single-arm NCT04429191 trial will assess 3 planned dose cohorts of JSP191 (0.3, 0.6, and 1.0 mg/kg) as a conditioning agent in patients with myelodysplastic syndromes and acute myeloid leukemia who are undergoing blood or hematopoietic cell transplantation.

• JSP191 is a humanized antibody targeting CD117.

BLAs of two antibody therapeutics submitted

On September 18, 2020, Agenus Inc. announced the initiation of the rolling submission of its Biologics License Application (BLA) to the FDA for balstilimab monotherapy for the treatment of recurrent/metastatic cervical cancer. In a Phase 2 study, patients treated with balstilimab (anti-PD-1) monotherapy achieved response rates of 19% in PD-L1 positive patients and 14% in all treated patients.

• Balstilimab is a human anti-PD-1 IgG4k antibody.

On September 21, 2020, ADC Therapeutics SA announced the submission of a **BLA to the FDA for loncastuximab tesirine** for the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma. In a pivotal Phase 2 study, patients who received the antibody-drug conjugate (ADC) demonstrated an overall response rate of 48.3% (70/145 patients) and a complete response rate of 24.1% (35/145 patients).

• Loncastuximab tesirine is composed of an anti-CD19 humanized antibody conjugated through a linker to a pyrrolobenzodiazepine dimer cytotoxin.

Cetuximab saratolacan approved in Japan

On September 25, 2020, Rakuten Medical Inc. announced that its wholly owned subsidiary Rakuten Medical Japan K.K. has received marketing approval in Japan from the Ministry of Health, Labour and Welfare for Akalux® IV Infusion 250mg (cetuximab saratolacan sodium) to treat unresectable locally advanced or recurrent head and neck cancer. BioBlade® Laser System, the medical device used in the combination with Akalux, was also approved on September 2nd. This combination was developed under the Rakuten Medical Illuminox[™] platform. Akalux received Sakigake Designation in April 2019, and application for approval under the Conditional Early Approval System was made in March 2020. Outside of Japan, Rakuten Medical does not have approval of its investigational therapies and is currently running a global Phase 3 trial.

 Cetuximab saratolacan sodium is composed of cetuximab, an anti-EGFR IgG1 antibody, conjugated to IRDye700DX, which is activated with a laser at the tumor site to induce rapid cancer cell destruction.

New FDA designations announced

Numerous companies have recently announced that FDA granted Breakthrough

Therapy, Fast Track, Orphan Drug or Rare Pediatric Disease designations for antibody therapeutics in their pipelines. These designations provide benefits designed to facilitate the discovery, non-clinical and clinical development, or regulatory review of the drugs.

Breakthrough Therapy designations

- On September 15, 2020, Gilead Sciences, Inc. announced that FDA granted Breakthrough Therapy designation for magrolimab, a humanized anti-CD47 IgG4k antibody, for treatment of newly diagnosed myelodysplastic syndrome. The safety and efficacy of magrolimab + azacitidine vs azacitidine + placebo in untreated participants with myelodysplastic syndrome are being evaluated in the Phase 3 ENHANCE study (NCT04313881).
- On September 25, 2020, RemeGen Co., Ltd. announced that the FDA has granted Breakthrough Therapy designation for disitamab vedotin (RC48-ADC), a humanized anti-HER2 IgG1k ADC, for the second-line treatment of patients with human epidermal receptor growth factor (HER)2positive locally advanced or metastatic urothelial cancer who have also previously received platinum-containing chemotherapy treatment.
 Disitamab vedotin is being evaluated in Phase 2 studies of patients with urothelial cancer, biliary tract cancer, and breast cancer.

Fast Track designation

 On September 24, 2020, Leap Therapeutics, Inc. announced that the FDA granted Fast Track designation to DKN-01 for the treatment of patients with gastric and gastroesophageal junction (G/GEJ) adenocarcinoma whose tumors express high Dickkopf-1 protein (DKK1), following disease progression on or after prior fluoropyrimidine- and platinum- containing chemotherapy and if appropriate, HER2/neu-targeted therapy. DKN-01, a humanized IgG4 antibody that binds to and blocks the activity of DKK1, a modulator of Wnt/Beta-catenin signaling, is being evaluated in Phase 1/2 or Phase 2 clinical trials for gastroesophageal, gynecologic, hepatobiliary, and prostate cancers.

Fast Track + Orphan Drug designation

 On September 28, 2020, AbbVie announced that the FDA granted Fast Track and Orphan Drug designations for elezanumab (ABT-555), a human IgG1 lambda antibody that binds to repulsive guidance molecule A, as a treatment for patients following spinal cord injury. Elezanumab is being investigated in Phase 2 studies of patients with spinal cord injuries, multiple sclerosis and acute ischemic stroke.

Orphan Drug designation

 On September 15, 2020, Kiniksa Pharmaceuticals, Ltd announced that the FDA granted Orphan Drug designation to mavrilimumab, is a human IgG4 lambda antibody targeting granulocyte macrophage colony stimulating factor receptor alpha, for the treatment of giant cell arteritis. Mavrilimumab undergoing evaluation in a Phase 2 study of patients with giant cell arteritis, as well as a Phase 2/3 study of patients with COVID-19.

Rare Pediatric Disease designation

 On September 24, 2020, Mereo BioPharma Group plc announced that the FDA has granted Rare Pediatric Disease designation to setrusumab, humanized monoclonal antibody that inhibits sclerostin, for the treatment of osteogenesis imperfecta (OI). OI is a genetic rare disorder with no approved treatments that is characterized by reduced bone mass and fragile bones that break easily. Positive results were observed in the Phase 2b ASTEROID study of setrusumab in adults with OI, and the company indicated that FDA and EMA have agreed on the principles of a design of a Phase 3 pediatric study in OI.

Antibody News You Should Know

October 1 - 15, 2020



COVID-19 intervention news

Preclinical results for anti-SARS-CoV-2 DARPins

On October 6, 2020, Molecular Partners AG announced supportive preclinical data from in vivo assessments of **two DARPin® candidates targeting SARS-CoV-2**. In a highly susceptible COVID-19 challenge model, hamsters were first infected with SARS-CoV-2 and then administered either select doses of MP0420 or MP0423, or placebo, at either 0, 6, or 24 hours. In the five-day experiment, all animals treated with DARPin® molecules recovered and survived, while 83% of animals in the placebo group experienced severe disease progression and were euthanized. First-in-human studies for MP0420 and MP0423 are planned in November 2020 and H1 2021, respectively.

 MP0420 and MP0423 trispecific anti-SARS-CoV-2 DARPin® molecules. MP0420 targets three different epitopes of the viral receptor-binding domain (RBD) simultaneously, and MP0423 targets three different parts of the coronavirus spike protein simultaneously. These include: the RBD, S1 N-terminal domain and S2 domain.

First clincal study of anti-SARS-CoV-2 STI-2020 to start

Details for a Phase 1/2 study (NCT04584697) to evaluate the safety, pharmacokinetics and efficacy of STI-2020 (COVI-AMG[™]) in outpatients with COVID-19 who are asymptomatic or have mild symptoms were posted on October 13, 2020. Patients will receive a single injection of 40 mg, 100 mg, or 200 mg of STI-2020. Due to start in December 2020, the study is not yet recruiting patients. The sponsor is Sorrento Therapeutics, Inc.

• STI-2020 is a human SARS-CoV-2 neutralizing monoclonal antibody.

Late-stage studies of anti-SARS-CoV-2 antibodies

On October 6, 2020, Vir Biotechnology, Inc. and GlaxoSmithKline plc announced the global expansion to Phase 3 of the COMET-ICE study (NCT04545060) evaluating VIR-7831 (GSK4182136) for the early treatment of COVID-19 in patients who are at high risk of hospitalization. Results for the primary endpoint, which is the proportion of patients who have progression of COVID-19 through Day 29, may be available as early as January 2021.

 VIR-7831 is a human antiSARS-CoV-2 neutralizing monoclonal antibody. The antibody was engineered with the potential to enhance lung bioavailability and have an extended half-life.

On October 9, 2020, AstraZeneca announced that **AZD7442**, **will advance into two Phase 3 clinical trials** in more than 6,000 participants at sites in and outside the US that are due to begin in the next weeks. AZD7442 was engineered with AstraZeneca's proprietary half-life extension technology to increase the durability of the therapy for six to 12 months following a single administration.

 AZD7442 is composed of two human anti-SARS-CoV-2 antibodies (AZD8895 + AZD1061) with half-life extension and reduced Fc receptor binding. On October 12, 2020, Celltrion Group announced the launch of its **Phase 3 clinical trial investigating CT-P59, a human anti-SARS-CoV-2 monoclonal antibody** as a preventative measure. The Phase 3 trial is set to enroll approximately 1,000 subjects to evaluate protective efficacy in contacts of SARS-CoV-2 infected patients.

On October 14, 2020, Eli Lilly and Company issued a **statement regarding ACTIV-3 (NCT04501978)**, an independent, NIH-sponsored study in hospitalized patients testing bamlanivimab (LY3819253, LYCoV555) in combination with remdesivir. The independent data safety monitoring board has recommended a pause to the study. Lilly's other ongoing studies, which focus on earlier stages of COVID-19 disease or prophylaxis, are not affected.

• Bamlanivimab is a human IgG1 antibody directed against the spike protein of SARS-CoV-2.

Emergency use authorizations requested for anti-SARS-CoV-2 antibodies

On October 7, 2020, Eli Lilly and Company and Regeneron announced that they have submitted requests to the U.S. Food and Drug Administration (FDA) for emergency use authorizations (EUA) of their anti-SARS-CoV-2 monoclonal antibodies.

 Lilly's EUA request is for bamlanivimab (LY-CoV555) monotherapy in higher-risk patients who have been recently diagnosed with mild-tomoderate COVID-19. According to the company, up to 100,000 doses of 700 mg LY-CoV555 monotherapy may be available in October, and one million doses available in Q4 2020. The combination of LY-CoV555 and LY-CoV016, which bind complementary regions of the SARS-CoV-2 spike protein, for the treatment of symptomatic COVID-19 in an outpatient setting is also being evaluated. Lilly anticipates submission of an EUA request for combination therapy in November, and may have data to support a biologics license application submission for combination therapy as early as Q2 2021.

 Regeneron's EUA request is for REGN-COV2, which is a combination of two anti-SARS-CoV-2 monoclonal antibodies (REGN10933 and REGN10987). Regeneron was granted a \$450 million contract to manufacture and supply REGN-COV2 by the US government, which has committed to making the doses available to Americans for free. The agreement covers a fixed number of bulk lots that are intended to be completed in the fall of 2020, as well as fill/finish and storage activities. At the time of the EUA request, Regeneron had doses available for ~ 50,000 patients, and expects to have doses available for a total of 300,000 patients within several months.

Updates on non-COVID-19 interventions

FDA and EMA actions in the news

On October 5, 2020, Y-mAbs Therapeutics, Inc. announced that the FDA issued a **Refusal to File letter regarding the Biologics License Application (BLA) for 1311-omburtamab** for the treatment of pediatric patients with CNS/leptomeningeal metastasis from neuroblastoma, which was submitted in August 2020. FDA determined that certain parts of the Chemistry, Manufacturing and Control and the Clinical modules of the BLA require further detail, but no additional non-clinical data have been requested or are required. Y-mAbs Therapeutics intends to re-submit the BLA by the end of 2020.

• 131I-Omburtamab is a murine IgG1 labeled with the radioisotope I-131.

On October 8, 2020, Elusys Therapeutics, Inc. announced that the European Medicines Agency's Committee for Medicinal Products for Human Use adopted a positive opinion recommending marketing authorization under exceptional circumstances for obiltoxaximab for the treatment of inhalation anthrax. The European Commission is expected to issue a final decision on the marketing authorization for obiltoxaximab in November 2020. Obiltoxaximab (ANTHIM®) was approved by FDA for this indication in March 2016.

• Obiltoxaximab is a deimmunized IgG1 antibody that targets the protective antigen of B. anthracis exotoxin.

On October 14, 2020, **FDA approved the triple antibody cocktail of atoltivimab, maftivimab, and odesivimab-ebgn (Inmazeb)** for the treatment for Zaire ebolavirus (Ebola virus) infection in adult and pediatric patients. FDA granted the atoltivimab, maftivimab, and odesivimab cocktail Breakthrough Therapy and Orphan Drug designations for the approved indication. Inmazeb was developed by Regeneron.

• Atoltivimab, maftivimab, and odesivimab are IgG1 antibodies that bind glycoprotein on the surface of Ebola virus, thereby blocking attachment and entry of the virus into cells.

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Antibody News You Should Know

October 15 - November 1, 2020



COVID-19 intervention news

Preclinical anti-SARS-CoV-2 targeted therapeutics

On October 19, 2020, Aridis Pharmaceuticals reported positive **preclinical efficacy data for inhaled AR-711** (originally known as1212C2) that supports a proposed self-administered therapy for COVID-19 patients. AR-711 eliminated detectable SARS-CoV-2 virus at all dose levels tested, with the lowest lung deposited dose of 0.03 mg/kg, in a golden Syrian hamsters challenge study where the animals were pre-infected with SARS-CoV-2 before a single inhalation exposure of the antibody. The company plans to start a Phase 1 study of AR-711 in non-hospitalized mild to moderate COVID-19 patients in H1 2020.

 AR-711 is a human IgG1 antibody derived from B-cells of convalescent COVID-19 patients. The antibody targets the conserved receptor-binding domain (RBD) region of SARS-CoV2.

On October 22, 2020, the International AIDS Vaccine Initiative (IAVI) and Serum Institute of India Pvt. Ltd. announced an **agreement with Merck KGaA to develop SARS-CoV-2 neutralizing monoclonal antibodies that were co-** **invented by IAVI and Scripps Research.** The partners will conduct preclinical and clinical research to evaluate the antibodies for treatment of COVID-19, and expect to start a Phase I clinical study early in 2021.

On October 28, 2020, **Novartis and Molecular Partners AG announced an option and license agreement to develop, manufacture and commercialize Molecular Partners' therapeutic candidates, MP0420 and MP0423**, for COVID-19. Molecular Partners will conduct Phase 1 clinical trials for MP0420, expected to begin in November 2020, and perform all remaining preclinical work for MP0423. Novartis will conduct Phase 2 and Phase 3 clinical trials, with Molecular Partners as sponsor of these trials. Upon option exercise, Novartis would be responsible for all further development and commercialization activities.

 MP0420 and MP0423 are tri-specific DARPin molecules. MP0420 targets three different epitopes of the RBD simultaneously, and MP0423 targets three different parts of the coronavirus spike protein (RBD, S1 N-terminal domain and S2 domain) simultaneously.

Phase 1 studies of anti-SARS-CoV-2 antibodies

Details for a **Phase 1 study (NCT04590430) of HFB30132A** were posted on October 19, 2020. HiFiBio is sponsoring this randomized, double-blind, placebocontrolled, single ascending dose first-in-human study investigating the safety, tolerability, and pharmacokinetics of intravenously administered HFB30132A in healthy adult subjects. An estimated 24 participants will be enrolled, and the study's primary completion date is in December 2020.

• HFB30132A is a SARS-CoV-2 neutralizing antibody.

On October 20, 2020, Abpro Corporation announced that **all subjects have been dosed in its Phase 1 clinical trial of ABP 300**. The Phase 1 clinical study is evaluating the safety of ABP 300 in 42 healthy subjects. Study results are expected in Q1 2021. • ABP 300 is a human antibody that binds the RBD of SARS-CoV-2.

Updates on LY-CoV555 and REGN-COV2 for COVID-19

LY-CoV555 and REGN-COV2 are anti-SARS-CoV-2 antibody therapies undergoing evaluation by the US Food and Drug Administration for possible emergency use authorization (EUA).

LY-CoV555 news announced October 28, 2020

- The New England Journal of Medicine published data from the monotherapy arms of BLAZE-1, a Phase 2 study assessing the efficacy and safety of Eli Lilly and Company's bamlanivimab (LY-CoV555) in the COVID-19 outpatient setting. The study data showed bamlanivimab may be effective in treating COVID-19 by reducing viral load, symptoms and the risk of hospitalization in outpatients.
- Eli Lilly and Company announced an initial agreement with the U.S. government to supply 300,000 vials of bamlanivimab 700 mg for \$375 million. The U.S. government will accept the vials of bamlanivimab if it is granted an EUA by the FDA. Lilly submitted a request for an EUA for bamlanivimab for the treatment of mild to moderate COVID-19 in high-risk patients to the FDA in early October.
- Lilly announced that they will offer bamlanivimab monotherapy at \$1,250
 per vial to wealthy countries, if authorized by the country's regulators.
 They will pursue tiered pricing arrangements for government purchases,
 based on the World Bank's gross national income per capita data. The
 pricing will be tiered based on countries' ability to pay, with wealthy
 countries paying the same as one another, middle-income countries
 receiving a steep discount, and the poorest countries paying only marginal
 costs.

REGN-COV2 news

On October 28, 2020, Regeneron Pharmaceuticals, Inc. announced positive, prospective results from an ongoing Phase 2/3 seamless trial in the COVID-19 outpatient setting showing its investigational cocktail of 2 antibodies, REGN-COV2, met the primary and key secondary endpoints. REGN-COV2 significantly reduced viral load and patient medical visits (hospitalizations, emergency room, urgent care visits and/or physician office/telemedicine visits). Regeneron has shared these results with the FDA, which is reviewing an EUA submission for the REGN-COV2 low dose (2.4 g) in adults with mild-to-moderate COVID-19 who are at high risk for poor outcomes.

Updates on non-COVID-19 interventions

New antibody in preclinical development

On October 19, 2020, NGM Biopharmaceuticals, Inc. announced the expansion of its oncology portfolio with its first immuno-oncology development candidate, **NGM707**, a novel dual antagonist antibody that inhibits Immunoglobulin-like transcript 2 (ILT2) and Immunoglobulin-like transcript 4 (ILT4). Targeting these key myeloid and lymphoid checkpoints may restrict anti-tumor immunity, enable tumors to evade immune detection and contribute to T cell checkpoint resistance.

 NGM Biopharmaceuticals plans to initiate first-in-human testing of NGM707 in mid-2021.

Phase 1 studies planned or initiated

Details for a **Phase 1/2 study (NCT04590326) of REGN5668** administered in combination with cemiplimab or REGN4018 in adult women with recurrent ovarian cancer were posted on October 19, 2020. This study is not yet recruiting

patients. The estimated enrollment is 290 patients, and the estimated study start date is November 20, 2020.

 REGN5668 is a costimulatory bispecific antibody targeting MUC16 and CD28.

On October 22, 2020, Daiichi Sankyo Company, Limited, announced that the first patient has been dosed in a **first-in-human study (NCT04419532) evaluating DS-1055** in patients with advanced or metastatic solid tumors who have progressed on standard treatments, including checkpoint inhibitors.

 DS-1055 is a monoclonal antibody designed to target GARP (Glycoprotein-A Repetitions Predominant), a transmembrane protein expressed on the surface of activated Tregs in the tumor microenvironment.

On October 26, 2020, NBE-Therapeutics announced that it has commenced a **first-in-human study (NCT04441099) of NBE-002** in patients with triple negative breast cancer and other solid tumors. Initial results from the study are expected in 2021.

 NBE-002 is an antibody-drug conjugate (ADC) composed of a humanized monoclonal antibody directed against receptor tyrosine kinase-like orphan receptor 1 (ROR1) that is site-specifically conjugated to a derivative of the highly potent anthracycline PNU-159682.

Phase 2 study of VLS-101 initiated

On October 19, 2020, VelosBio Inc. announced that the **first patient has been dosed in a Phase 2 trial (NCT04504916) of VLS-101** in patients with solid tumors. This study will assess one dose level (2.5 mg/kg) of VLS-101 administered intravenously in repeated 21-day cycles.

• VLS-101 is an ADC composed of a humanized anti-ROR1 antibody conjugated via a proteolytically cleavable linker to monomethyl auristatin E.

Phase 3 study of monalizumab initiated

On October 23, 2020, Innate Pharma SA announced that AstraZeneca has **dosed the first patient in its Phase 3 clinical trial (NCT04590963; INTERLINK-1) evaluating monalizumab** in combination with cetuximab in patients with recurrent or metastatic squamous cell carcinoma of the head and neck who have been previously treated with platinum-based chemotherapy and PD-(L)1 inhibitors.

 Monalizumab is a humanized IgG4 antibody that targets NKG2A, is an inhibitory member of the NKG2 family expressed on CD56hi natural killer cells.

Update on MAA for aducanumab

On October 30, 2020, Biogen and Eisai, Co., Ltd. announced that the European Medicines Agency has confirmed it has **accepted for review, following a standard timetable, the Marketing Authorization Application for aducanumab**, an investigational treatment for Alzheimer's disease. Aducanumab is also under FDA review, and the application's action date is March 7, 2021. An FDA advisory committee meeting is scheduled for November 6, 2020.

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

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Antibody News You Should Know

November 1 - 15, 2020



COVID-19 intervention news

IND filed for anti-SARS-CoV-2 STI-2020

On November 9, 2020, Sorrento Therapeutics, Inc. announced that it is filing an **investigational new drug application for intravenous COVI-AMG (STI-2020) to treat COVID-19** patients with mild symptoms and to evaluate safety and pharmacokinetics in healthy volunteers. Sorrento is also developing an intranasal formulation of COVI-AMG[™] called COVI-DROPS (STI-2099).

• STI-2020 is human SARS-CoV-2 neutralizing monoclonal antibody. It is an affinity-matured derivative of COVI-Guard (STI-1499), which is already undergoing evaluation in a Phase 1 study (NCT04454398).

Positive Phase 1 results for CT-P59

On November 5, 2020, Celltrion Group announced **results from the ongoing placebo-controlled Phase I clinical study of CT-P59**, which demonstrated a promising safety, tolerability, antiviral effect, and efficacy profile in patients with mild symptoms of COVID-19. CT-P59 was dosed at 20 mg/kg, 40 mg/kg or 80 mg/kg, with 5 patients in each dose cohort. Patients treated with CT-P59

experienced about 44% reduced mean clinical recovery time in comparison to the average placebo recovery time.

• CT-P59 is a human anti-SARS-CoV-2 antibody derived from the B cells of convalescent patients.

FDA authorizes emergency use of anti-SARS-CoV2 LY-CoV555 for COVID-19

On November 9, 2020, the US Food and Drug Administration authorized the emergency use of anti-SARS-CoV-2 bamlanivimab (LY-CoV555, LY3819253). The agency stated that "it is reasonable to believe that bamlanivimab may be effective for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization, and that, when used under the conditions described in this authorization, the known and potential benefits of bamlanivimab when used to treat COVID-19 in such patients outweigh the known and potential risks of such product."

 Bamlanivimab is a human IgG1 antibody directed against the receptor binding domain of the spike protein of the SARS-CoV-2 coronavirus. AbCellera and Eli Lilly and Company partnered on the discovery and development of the antibody, which was derived from B cells of convalescent patients.

CAN-COVID trial of canakinumab (ILARIS®) does not meet endpoints

On November 6, 2020, Novartis announced that the Phase 3 placebo-controlled CAN-COVID trial (NCT04362813) evaluating the efficacy and safety of **canakinumab plus standard of care in hospitalized patients with COVID-19 pneumonia and cytokine release syndrome did not meet its primary endpoint** of a greater chance of patient survival without the need for invasive mechanical ventilation, or its key secondary endpoint of reduced COVID-19 mortality, compared with standard of care only.

 Canakinumab (ILARIS®), a monoclonal antibody that targets interleukin-1 beta, is approved in ~ 60 countries, including the US, and EU, for rare conditions, including periodic fever syndromes, adult-onset Still's disease and systemic juvenile idiopathic arthritis.

Updates on non-COVID-19 interventions

First-in-human studies for 3 antibodies to start

Details of an open-label, single-arm, dose-escalation study (**NCT04622774**) of IMGC936 in patients with advanced solid tumors were posted on November 10, 2020. IMGC936 will be administered every 3 weeks. Sponsored by ImmunoGen and MacroGenics, this study is recruiting patients. The estimated primary completion date is in July 2021.

 IMGC936 is antibody-drug conjugate composed of indolinobenzodiazepine DNA-alkylating monoimine conjugated to engineered cysteine residues of a humanized anti-ADAM9 antibody via a peptide linker (drug-to-antibody ratio of 2).

On November 11, 2020, the rationale for target patient population and **first-in-human trial design of W0180** were presented at the 2020 Society for Immunotherapy of Cancer annual meeting. Sponsored by Pierre Fabre Medicament, the Phase 1 study (NCT04564417) will evaluate W0180 as single agent and in combination with pembrolizumab (anti-PD-1) in adult participants with locally advanced or metastatic solid tumors.

• W0180 is a monoclonal antibody that targets V-domain Ig Suppressor of T-cell Activation (VISTA).

Details of a Phase 1/2 study (NCT04626635) of REGN7075 in combination with cemiplimab in patients with advanced solid tumors were posted on November 12, 2020. REGN7075 will be administered every week or every 3 weeks via IV infusion. Due to start on November 17, 2020, the study has an estimated primary completion date in January 2025.

• REGN7075 is a costimulatory bispecific antibody that targets epidermal growth factor receptor and CD28.

Phase 2 study of JNJ-63733657 to start

Details of a placebo-controlled Phase 2 study (**NCT04619420**) of Janssen's JNJ-63733657 in participants with early Alzheimer's disease were posted on November 10, 2020. Participants will receive a single low or high dose of JNJ-63733657 administered by intravenous infusion every 4 weeks. The estimated primary completion date is January 8, 2025. This study is due to start in November 2020.

 JNJ-63733657 is a monoclonal antibody that targets the mid-region of tau, and thereby it may more potently interfere with cell-to-cell propagation of pathogenic, aggregated tau than do antibodies targeting the tau Nterminus.

Phase 3 study of epcoritamab to start

Details of a Phase 3 study (NCT04628494) of epcoritamab (GEN3013; DuoBody®-CD3xCD20) in diffuse large B-cell lymphoma (DLBCL) were posted on November 13, 2020. The study will evaluate the efficacy and safety of subcutaneous epcoritamab vs. investigators' choice of chemotherapy in patients with relapsed or refractory DLBCL. Epcoritamab is being co-developed by Genmab and AbbVie. • Epcoritamab is a human IgG1 bispecific antibody that targets CD3 and CD20.

FDA Advisory Committee votes on aducanumab study data

In an advisory meeting on November 6, 2020, most members of FDA's **Peripheral and Central Nervous System Drugs Advisory Committee voted that the study data did not support aducanumab's efficacy**. The 4 questions the members considered were:

1) Does Study 302 (EMERGE), viewed independently and without regard for Study 301 (ENGAGE), provide strong evidence that supports the effectiveness of aducanumab for the treatment of Alzheimer's disease? (votes: 1 yes, 8 no and 2 uncertain);

2) Does Study 103 (PRIME) provide supportive evidence of the effectiveness of aducanumab for the treatment of Alzheimer's disease? (votes: 0 yes, 7 no and 4 uncertain);

3) Has the Applicant presented strong evidence of a pharmacodynamic effect of aducanumab on Alzheimer's disease pathophysiology?" (votes: 5 yes, 0 no and 6 uncertain); and

4) In light of the understanding provided by the exploratory analyses of Study 301 and Study 302, along with the results of Study 103 and evidence of a pharmacodynamic effect on Alzheimer's disease pathophysiology, it is reasonable to consider Study 302 as primary evidence of effectiveness of aducanumab for the treatment of Alzheimer's disease? (votes: 0 yes, 10 no and 1 uncertain).

FDA typically follows the advice of their advisory committees, but there have been exceptions in the past.

• Aducanumab (BIIB037) is an anti-amyloid beta IgG1k antibody.

FDA issues a Complete Response Letter regarding sutimlimab's BLA

On November 14, 2020, Sanofi announced that FDA issued a Complete

Response Letter regarding for sutimlimab's Biologics License Application. No clinical or safety deficiencies were noted in the letter, but certain deficiencies were identified by FDA during a pre-license inspection of a third-party facility responsible for manufacturing. Sanofi is working to resolve the issues in a timely fashion.

• Sutimlimab is a humanized IgG4 antibody that targets and inhibit C1s in the classical complement, thereby interfering with C1-activated hemolysis in cold agglutinin disease.

Attending a virtual meeting soon?

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

8th Antibody Industrial Symposium, Nov. 23-24, 2020

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PepTalk: The Protein Science and Production Week, Jan 19-20, 2021

Antibody News You Should Know

November 15 - December 1, 2020



COVID-19 intervention news

Preclinical data for anti-SARS-CoV-2 antibodies

On November 23, 2020 **Twist Bioscience Corporation announced preclinical data** for three of its proprietary antibodies against the S1 protein of SARS-CoV-2. TB202-3 and TB202-63 protected against weight loss at the lowest dose of 1 mg/kg in a preclinical hamster challenge model, and TB181-36 was found to protect against weight loss at 5 mg/kg and 10 mg/kg.

- TB202-63 and TB202-3 are single domain VHH nanobodies that bind the S1 receptor binding domain; both were identified by Twist Biopharma.
- TB181-36 is an IgG antibody derived from convalescent patients in a collaborative research project with Vanderbilt University Medical Center researchers James E. Crowe, Jr and Robert Carnahan in the Vanderbilt Vaccine Center. TB181-36 binds a unique epitope on the N terminal domain of S1.

New anti-SARS-CoV-2 antibodies to start first-in-human studies On November 18, 2020, CORAT Therapeutics announced the completion of the production campaign for anti-SARS-CoV-2 antibody COR-101. Their rapid production process is based on stable expressing CHO cell pools. CORAT Therapeutics plans on starting clinical studies of COR-101 in early 2021.

On November 17, 2020, details were posted on clinical trials.gov for two Phase 1/2a trials of the inhaled administration (**NCT04631705**) or intravenous administration (**NCT04631666**) of DZIF-10c in SARS-CoV-2-infected and - uninfected individuals. Sponsored by the University of Cologne with their collaborator Boehringer Ingelheim, the two studies will each enroll an estimated 69 patients.

• DZIF-10c is a human monoclonal SARS-CoV-2-neutralizing antibody.

On November 25, 2020, details were posted on clinical trials.gov for a Phase 1 randomized, double-blind, placebo-controlled, study to evaluate the safety, pharmacokinetics, and pharmacodynamics of single ascending doses of ABBV-47D11 in adults hospitalized with COVID-19. Sponsored by AbbVie, the **NCT04644120** study will enroll an estimated 24 patients.

• 47D11, a fully human, SARS-CoV-2-neutralizing antibody was discovered by Harbour BioMed, Utrecht University and Erasmus Medical Center.

First patients dosed with new anti-SARS-CoV-2 targeted therapeutic

On November 23, 2020, Molecular Partners AG announced that a first cohort of eight healthy volunteers has been dosed in a **Phase 1 first-in-human study of MP0420** (ensovibep), a DARPin® therapeutic candidate for the potential treatment and prevention of COVID-19. MP0420 will be intravenously administered in up to 24 healthy volunteers divided into three dose cohorts, with each cohort stratified 3:1 in favor of MP0420.

Late-stage clinical study of anti-SARS-CoV-2 SCTA01 to start

On November 25, 2020, details were posted on clinical trials.gov for a Phase 2/3 trial to evaluate the efficacy and safety of SCTA01 in hospitalized patients with

severe COVID-19. Sponsored by Sinocelltech Ltd., the **NCT04644185** study will enroll an estimated 795 patients.

 SCTA01 is a recombinant anti-SARS-CoV-2 spike protein monoclonal antibody

Casirivimab + imdevimab cocktail granted emergency use authorization in the US

On November 20, 2020, the US Food and Drug Administration (FDA) authorized the emergency use of casirivimab and imdevimab (REGN-COV2) for 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 progressing to severe COVID-19 and/or hospitalization. This antibody cocktail has been shown to reduce COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo. The authorized dosage is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous (IV) infusion over at least 60 minutes via pump or gravity as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset.

 Casirivimab and imdevimab are recombinant human IgG1 monoclonal antibodies that target the receptor binding domain of the spike protein of SARS-CoV-2.

Updates on non-COVID-19 interventions

IND and first-in-human study news

On November 16, 2020 during SeaGen's R&D Day presentation, the company disclosed that an **Investigational New Drug (IND) application for SGN-STNV**

had been submitted in November 2020 and a Phase 1 trial was planned for early Q1 2021.

• SGN-STNV is a Sialyl Thomsen-nouveau (STn)-targeted vedotin ADC with preclinical activity across multiple solid tumors.

On November 16, 2020, Jounce Therapeutics, Inc. announced the company has received a **Study May Proceed Letter from the FDA to begin a Phase 1 trial, named INNATE, for JTX-8064.** This study will evaluate JTX-8064 as monotherapy and in combination with Jounce's PD-1 inhibitor, JTX-4014, or with pembrolizumab in patients with solid tumors.

 JTX-8064 is an anti-Leukocyte Immunoglobulin Like Receptor B2 (LILRB2/ILT4) antibody.

On November 19, 2020, details were posted on clinical trials.gov for a Phase 1 study of LVGN7409 as single agent and combination therapies in advanced or metastatic malignancy. Sponsored by Lyvgen Biopharma Holdings Limited, the **NCT04635995** study will enroll an estimated 126 patients.

• LVGN7409 is an anti-CD40 agonist antibody.

On November 26, 2020, details were posted on clinical trials.gov for a Phase 1 dose escalation study of ADG126 in patients with advanced malignancies. Sponsored by Adagene Inc., the **NCT04645069** study will enroll an estimated 100 patients.

 ADG126 is a human anti-CTLA-4 SAFEbody designed to address the safety concerns associated with existing CTLA-4 therapeutics. It is designed to enhance the safety features by masking the antibody binding site, which would be unmasked in the tumor micro-environment. On December 1, 2020, Junshi Biosciences announced that the China National Medical Products Administration has accepted its IND application for JS006.

 JS006 is a recombinant humanized IgG4κ monoclonal antibody against human TIGIT.

BLA for loncastuximab tesirine granted priority review

On November 20, 2020, ADC Therapeutics SA announced that the FDA has accepted its Biologics License Application for loncastuximab tesirine for the treatment of relapsed or refractory diffuse large B-cell lymphoma and granted priority review status. The FDA has set a first action target date of May 21, 2021.

 Loncastuximab tesirine is an ADC composed of an anti-CD19 humanized monoclonal antibody conjugated through a linker to a pyrrolobenzodiazepine dimer cytotoxin.

FDA approves naxitamab-gqgk

On November 25, 2020, **FDA approved naxitamab-gqgk (DANYELZA®)** 40mg/10ml in combination with granulocyte-macrophage colony-stimulating factor for the treatment of pediatric patients 1 year of age and older and adult patients with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy. The approval for this indication was granted under FDA's accelerated approval regulations based on the overall response rate and duration of response.

• Naxitamab, a humanized anti-GD2 IgG1k antibody, was developed by Memorial Sloan Kettering Cancer Center and licensed to Y-mAbs.

Antibody News You Should Know

December 1 - 15, 2020



COVID-19 intervention news

New anti-SARS-CoV-2 antibodies enter the clinic

On December 9, 2020, Sorrento Therapeutics, Inc. announced that the **Food and Drug Administration (FDA) accepted the Investigational New Drug (IND) application** for a clinical study for intravenous STI-2020 (COVI-AMG). The placebo-controlled Phase 1/2 trial (NCT04584697) will evaluate the safety, pharmacokinetics and efficacy of a single injection of STI-2020 (40 mg, 100 mg, or 200 mg) in outpatient COVID-19 patients with mild symptoms.

 STI-2020 is a human SARS-CoV-2 neutralizing monoclonal antibody with binding affinity against viral variants is similar to or better than that observed for wild-type SARS-CoV-2.

On December 14, 2020, Harbour BioMed and Utrecht University announced that they licensed the 47D11 program to AbbVie, and that **AbbVie has initiated a Phase 1** clinical trial of the antibody. The Phase 1 study (NCT04644120) will evaluate the safety, pharmacokinetics, and pharmacodynamics of single ascending doses of ABBV-47D11 in adults hospitalized with COVID-19. A total of 3 doses will be evaluated. 47D11, also know an ABBV-47D11 and HBM9022, is a human SARS-CoV-2 neutralizing monoclonal antibody.

Phase 3 study of anti-SARS-CoV-2 antibody TY027 starts

On or about December 4, 2020, recruitment started for a Phase 3 multi-site, randomized, placebo controlled, double blind, single dose study (**NCT04649515**) of TY027 for early treatment of COVID-19. The study will evaluate 2 doses (1.5 g and 2 g) of TY027.

• TY027 is a SARS-CoV-2 neutralizing monoclonal antibody.

Updates on non-COVID-19 interventions

Acquisitions in the news

On December 10, 2020, **Boehringer Ingelheim announced the signing of a binding agreement for acquiring all shares of NBE-Therapeutics**, a private, clinical-stage Swiss biotechnology company focused on antibody-drug conjugates and advancing targeted cancer therapies derived from its immune stimulatory iADC[™] platform. NBE-Therapeutics' lead compound NBE-002 is currently in a Phase 1 clinical study for triple negative breast cancer and other solid tumors. Closing of the deal is anticipated in Q1 2020.

On December 12, 2020, AstraZeneca and Alexion Pharmaceuticals, Inc. announced that they have entered into a definitive agreement for **AstraZeneca to acquire Alexion**. Alexion's franchise includes Soliris (eculizumab), a first-in-class anti-complement component 5 (C5) monoclonal antibody approved in many countries for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome, generalized myasthenia gravis and neuromyelitis optica spectrum disorder. Alexion also launched Ultomiris (ravulizumab), a second-generation C5 monoclonal antibody with a more convenient dosing regimen. Alexion's clinical pipeline includes 2 antibodies, ALXN1830, which blocks neonatal Fc receptor-mediated recycling, and ALXN1720, a bispecific mini-body targeting C5.

First-in-human studies started

On December 3, 2020, F-star Therapeutics, Inc. announced that the first patient has been dosed in a **Phase 1 trial evaluating its bispecific antibody FS120**. The Phase 1 study (NCT04648202) will evaluate the safety, tolerability, pharmacokinetics, and activity of FS120 in patients with advanced malignancies.

• FS120 is a dual-agonist tetravalent bispecific antibody targeting CD137 (4-1BB, TNFRSF9) and OX40 (CD134, TNFRSF4).

On December 11, 2020, PureTech Health plc announced the initiation of its **Phase 1 clinical trial of LYT-200** for the potential treatment of metastatic solid tumors that are difficult to treat and have poor survival rates. NCT04666688 is a Phase 1/2 open-label, multi-center study of the safety, pharmacokinetics, and anti-tumor activity of LYT-200 alone and in combination with chemotherapy or anti-PD-1 in patients with metastatic solid tumors.

• LYT-200 is a human monoclonal antibody that targets galectin-9.

On December 15, 2020, Prometheus Biosciences, Inc. announced FDA acceptance of its IND for PRA023 and that dosing has **commenced in a Phase 1a clinical study** in normal healthy volunteers. Prometheus is developing PRA023 for ulcerative colitis and Crohn's disease.

• PRA023 is a humanized IgG1 monoclonal antibody that has been shown to block tumor necrosis factor-like ligand 1A (TL1A).

First Phase 3 studies initiated or due to start soon

On December 7, 2020, details were posted on clinicaltrials.gov for a multicenter, double-blind, randomized, placebo-controlled, parallel-arm Phase 3 study (**NCT04656418**) to investigate the efficacy and safety of subcutaneous administration of CSL312 (garadacimab) in the prophylactic treatment of hereditary angioedema. The estimated start date is January 2021; the estimated enrollment is 60 patients.

 Garadacimab is a human IgG4/lambda monoclonal antibody targeting Factor XIIa.

On December 9, 2020, details were posted on clinicaltrials.gov for a Phase 3 study (**NCT04658862**) evaluating the efficacy of TAR-200 in combination with cetrelimab (JNJ-63723283) versus concurrent chemoradiotherapy in participants with muscle-invasive urothelial carcinoma of the bladder who are not receiving radical cystectomy. TAR-200 is a gemcitabine intravesical delivery system that provides a continuous release of gemcitabine into the urine. The estimated start date is December 2020; the estimated enrollment is 550 patients.

• Cetrelimab is a human IgG4 monoclonal antibody targeting PD-1.

On December 14, 2020, Daiichi Sankyo Company, Limited and AstraZeneca announced the initiation of a global pivotal Phase 3 head-to-head study (NCT04656652, TROPION-Lung01) of datopotamab deruxtecan (DS-1062) versus docetaxel in patients with advanced or metastatic non-small cell lung cancer without actionable genomic alterations who have previously received platinum-based chemotherapy and immunotherapy. The estimated enrollment is 590 patients.

 Datopotamab deruxtecan is an antibody-drug conjugate composed of a humanized anti-TROP2 antibody conjugated to DX-8951, which is a topoisomerase I inhibitor.

5

Biologics license applications submitted

On December 1, 2020, TG Therapeutics, Inc. announced that they initiated a **rolling submission of a Biologics License Application (BLA) to the FDA requesting approval of ublituximab** in combination with umbralisib, a oncedaily, oral, dual inhibitor of PI3K-delta and CK1-epsilon, as a treatment for patients with chronic lymphocytic leukemia (CLL). The FDA previously granted Fast Track Designation to the combination of ublituximab and umbralisib for the treatment of adult patients with CLL and Orphan Drug Designation for ublituximab in combination with umbralisib for the treatment of CLL. TG Therapeutics expects to complete the BLA rolling submission in the first half of 2021.

• Ublituximab is a glycoengineered anti-CD20 monoclonal antibody.

On December 3, 2020, The Janssen Pharmaceutical Companies of Johnson & Johnson announced the **submission of a BLA to the FDA seeking approval of amivantamab** for the treatment of patients with metastatic non-small cell lung cancer with epidermal growth factor receptor (EGFR) exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy. In March 2020, amivantamab received Breakthrough Therapy Designation from the FDA for this population

• Amivantamab is a human bispecific antibody targeting EGFR and mesenchymal epithelial transition factor (MET).

Attending a virtual meeting soon?

Antibody News You Should Know

December 15, 2020 - January 1, 2021

Our best wishes for a happy and healthy new year in 2021 to you and yours!



COVID-19 intervention news

Preclinical results for anti-SARS-CoV-2 antibody COR-101

On December 18, 2020, CORAT Therapeutics GmbH reported the successful conclusion of hamster disease model tests of their **lead candidate COR-101 against COVID-19**. It induced recovery of SARS-CoV-2 infected hamsters within two days vs a full week for untreated animals. The company anticipates starting a first-in-humans study in January 2021.

• COR-101 is a human SARS-CoV-2-neutralizing monoclonal IgG antibody that binds a very broad area of the virus. The Fc region of COR-1010 was engineered to reduce its effector functions.

First-in-human study of anti-SARS-CoV-2 antibodies started

Details for a Phase 1, randomized, double-blind, placebo-controlled study

(NCT04669262) to evaluate the safety, tolerability, pharmacokinetics, and immunogenicity of BGB-DXP604 alone and in combination with BGB-DXP593 in healthy subjects were posted on clinicaltrials.gov on December 16, 2020. This study is recruiting patients and has an estimated primary completion date in March 2021.

 DXP-593 and DXP-604 are SARS-CoV-2-neutralizing antibody drug candidates identified by high-throughput single-cell RNA and VDJ sequencing of antigen-enriched B cells from convalescent patients

Late-stage studies of anti-SARS-CoV-2 antibodies started

On December 16, 2020, Abpro Corporation announced the initiation of global **Phase 2/3 registrational studies evaluating the safety, tolerability, efficacy, and pharmacokinetics of ABP 300**. ABP 300 will be delivered in a one-time dose across 3 treatment arms using a 1:1:1 randomization comparing a high dose, low dose, and placebo.

• ABP 300 is a human neutralizing antibody derived from convalescent patients.

On December 17, 2020, the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, announced that their Phase 3 ACTIV-3 master protocol has been expanded to include: 1) VIR-7831; and 2) the combination of BRII-196 and BRII-198. This master protocol is designed to evaluate the safety and efficacy of multiple investigational agents aimed at modifying the host immune response to SARS-CoV-2 infection, or directly enhancing viral control in order to limit disease progression. The anti-SARS-CoV-2 antibody LY3819253 and remdesivir were previously included in ACTIV-3.

- VIR-7831 is an anti-SARS-CoV-2 monoclonal antibody developed through a partnership between GlaxoSmithKline plc and Vir Biotechnology, Inc.
- BRII-196 and BRII-198 are two anti-SARS-CoV-2 monoclonal antibodies manufactured by Brii Biosciences.

Conditional Marketing Authorization requested for CT-P59

On December 29, 2020, Celltrion Group announced that the company had submitted a formal Application for **Conditional Marketing Authorization of CT-P59** to the Korean Ministry of Food and Drug Safety. This submission is based on the data from global Phase II/III clinical trial of CT-P59. The company plans to submit Emergency Use Authorization to the U.S. Food and Drug Administration (FDA) and Conditional Marketing Authorization to the European Medicines Agency for CT-P59 in the coming months.

• CT-P59 is a human neutralizing antibody derived from convalescent patients.

Updates on non-COVID-19 interventions

First-in-human studies starting soon

Details for a Phase 1 clinical study (**NCT04671875**) to evaluate safety, tolerability, pharmacokinetics and efficacy of MIL93 in advanced or metastatic solid tumors were posted on clinicaltrials.gov on December 17, 2020. The study is sponsored by Beijing Mabworks Biotech Co., Ltd. Due to start in February 2021, this study is not yet recruiting patients.

 MIL93 is a recombinant humanized anti-Claudin 18.2 IgG1 monoclonal antibody

On December 18, 2020, CANbridge Pharmaceuticals Inc. announced that its **Investigational New Drug application for CAN106** has been approved by the Health Sciences Authority in Singapore for the treatment of complement dysregulation diseases. The first indication is paroxysmal nocturnal hemoglobinuria.

• CAN106 a recombinant human monoclonal antibody targeting complement C5 of the complement system.

Phase 2/3 study of ANX005 started

On December 21, 2020, Annexon, Inc. announced that patient dosing has started in a **Phase 2/3 clinical study of ANX005** to treat Guillain-Barré Syndrome (GBS). GBS is a rare, acute, antibody-mediated autoimmune disease that affects the peripheral nervous system and can lead to acute paralysis and/or permanent disability from nerve loss. ANX005 has received Fast Track and Orphan Drug designations from the FDA for the treatment of GBS.

• ANX005 is a humanized IgG4 antibody that targets Complement C1q

FDA approves 2 novel antibody therapeutics

On December 16, 2020, the **US FDA approved margetuximab-cmkb** (MARGENZA), in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.

 MARGENZA is a chimeric IgG1 monoclonal antibody that binds to HER2. The antibody's modified Fc region increases binding to the activating Fc receptor CD16A and decreases binding to the inhibitory Fc receptor CD32B, which leads to greater in vitro antibody-dependent cell-mediated cytotoxicity and natural killer cell activation.

On December 21, 2020, the **US FDA approved ansuvimab-zykl (Ebanga)** for the treatment for Zaire ebolavirus infection in adults and children. Ebanga had been granted US Orphan Drug designation and Breakthrough Therapy designations.

• Ansuvimab is a human IgG1 monoclonal antibody that binds and neutralizes Ebolavirus.