September 15 - October 1, 2021



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### **COVID-19 intervention news**

#### **Emergency use authorization requested for BRII-196/BRII-198**

On October 8, 2021, **Brii Biosciences Limited announced** the filing of an emergency use authorization (EUA) application for BRII-196/BRII-198 with the U.S. Food and Drug Administration (FDA). The application is based on interim results from the Phase 2/3 ACTIV-2 trial. Data to support the EUA request will be submitted to FDA on a rolling basis. Sponsored by the National Institutes of Health, the ACTIV-2 study (NCT04518410) is a master protocol designed to evaluate the safety and efficacy of multiple investigational agents in COVID-19-positive adult outpatients. The combination of the two antibodies demonstrated a statistically significant reduction of 78% in the combined endpoint of hospitalization and death compared with placebo in the ACTIV-2 trial.

• Amubarvimab and romlusevimab (BRII-196 and BRII-198) are human IgG1 antibodies that target distinct epitopes of the SARS-CoV-2 spike protein.

### Updates on non-COVID-19 interventions

#### New antibody therapeutics queued for clinical study

On October 7, 2021, details were posted on clinical trials.gov for a Phase 1 study (**NCT05070247**) of TAK-500 as a single agent and in combination with pembrolizumab in adult patients with select locally advanced or metastatic solid tumors. Sponsored by Takeda, the study will enroll an estimated 106 patients and has an estimated start date of November 17, 2021.

 TAK-500 is a targeted antibody-drug conjugate (ADC) STING agonist with a payload of TAK-676, which is a small molecule STING agonist with an undisclosed structure that is now under clinical investigation in a Phase 1 dose escalation study.

On October 11, 2021, details were posted on clinical trials.gov for a Phase 1 study (**NCT05073484**) of BAT6021 as monotherapy or in combination with BAT1308 in patients with advanced solid tumors. Sponsored by Bio-Thera Solutions, the study will enroll an estimated 29 participants and has an estimated start date of October 1, although it was listed as not yet recruiting on October 14, 2021.

• BAT6021 is a humanized anti-TIGIT antibody, and BAT1308 is a humanized anti-PD-1 antibody.

On October 12, 2021, details were posted on clinical trials.gov for a Phase 1/2 study (**NCT05074472**) of ZB131 in solid tumors that are likely to express cancer-specific plectin (CSP). Sponsored by ZielBio, Inc., the study will enroll an estimated 37 participants and has an estimated start date of January 17, 2021.

• ZB131 is a CSP-targeting antibody.

On October 14, 2021, details were posted on clinical trials.gov for a Phase 1 dose-escalation study (**NCT05077423**) trial of CD33xCD3 bispecific antibody in pediatric patients with relapsed or refractory acute myeloid leukemia (AML). Sponsored by Y-mAbs Therapeutics, the study will enroll an estimated 37 participants and has an estimated start date of January 17, 2021.

• CD33xCD3 is a bispecific monoclonal antibody that specifically targets CD33 on the AML blasts and CD3 on the T cells.

#### First-in-human studies started

On October 4, 2021, **Compugen Ltd. announced** that Compugen is entitled to receive a \$6 million milestone payment from AstraZeneca triggered by the dosing of the first patient in a Phase 1/2 study evaluating AZD2936 in patients with advanced or metastatic non-small cell lung cancer. AZD2936 is derived from COM902, Compugen's high-affinity clinical-stage anti-TIGIT antibody.

• AZD2936 is an anti-TIGIT/PD-1 bispecific antibody.

On October 7, 2021, **Acumen Pharmaceuticals**, **Inc. announced** dosing of the first patient in INTERCEPT-AD, the Phase 1 placebo-controlled, single- and multiple-dose clinical trial of ACU193 for the treatment of early Alzheimer's disease. The study (NCT04931459) will enroll an estimated 62 patients mild cognitive impairment or mild dementia due to Alzheimer's disease.

 ACU193 is a monoclonal antibody that selectively targets toxic amyloidbeta oligomers.

#### First Phase 2 study of anti-CXCR5 antibody to start soon

On October 7, 2021, details were posted on clinical trials.gov for a Phase 2 study (**NCT05070845**) of PF-06835375 in adult participants with moderate to severe

primary immune thrombocytopenia. Sponsored by Pfizer, the study will enroll an estimated 40 participants and has an estimated start date of November 14, 2021.

 PF-06835375 is an antibody that targets C-X-C chemokine receptor type 5, also known as CD185 or Burkitt lymphoma receptor 1, which is a G protein-coupled seven transmembrane receptor for chemokine CXCL13 and belongs to the CXC chemokine receptor family.

## Lenzilumab Conditional Marketing Authorization application submitted

On October 1, 2021, **Humanigen, Inc. announced** it has submitted all the planned modules, as well as a risk management plan and pediatric investigation plan, for the Conditional Marketing Authorization of lenzilumab in hospitalized COVID-19 patients to the UK's Medicines and Healthcare Products Regulatory Agency (MHRA). MHRA has previously accepted the application for expedited COVID-19 rolling review.

• Lenzilumab is a human IgG1 antibody that binds to and neutralizes granulocyte-macrophage colony-stimulating factor.

# Relatlimab and nivolumab fixed-dose combo undergoing EMA review

On October 1, 2021, **Bristol Myers Squibb announced** that the European Medicines Agency (EMA) has validated its Marketing Authorization Application for the relatlimab and nivolumab (Opdivo®) fixed-dose combination for first-line treatment of adult and pediatric patients (12 years and older and weighing at least 40 kg) with advanced (unresectable or metastatic) melanoma. This validation confirms completion of the submission and begins the EMA's centralized review process.

• Relatlimab is a human IgG4 anti-LAG-3 antibody.

#### Decision on narsoplimab BLA delayed

On October 1, 2021, **Omeros Corporation announced** that the FDA notified the company that, as part of FDA's ongoing review of the company's Biologics License Application for narsoplimab in the treatment of hematopoietic stem cell transplant-associated thrombotic microangiopathy, FDA has identified deficiencies that preclude discussion of labeling and post-marketing requirements/commitments at this time. The company does not currently expect any such resolution to occur by the October 17, 2021, target action date.

• Narsoplimab is a human IgG4 antibody that targets mannan-binding lectinassociated serine protease-2.

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### **COVID-19 intervention news**

#### Clinical study of REGN14256 to start

On October 18, 2021, details were posted on clinical trials.gov for a Phase 1/2/3 adaptive study (**NCT05081388**) to evaluate the safety, tolerability, and efficacy of REGN14256+imdevimab for the treatment of COVID-19 patients without risk factors for progression to severe disease. Sponsored by Regeneron, the study will enroll an estimated 1,359 patients and has an estimated start date of October 20, 2021, although the record was listed as not yet recruiting when accessed on October 30, 2021.

 Imdevimab is an anti-SARS-CoV-2 antibody that, together with casirivimab, comprises REGN-COV, which currently is available in multiple countries on an emergency use basis. REGN14256 is presumably also an anti-SARS-CoV-2 antibody.

### **Updates on non-COVID-19 interventions**

#### New antibody therapeutic queued for clinical study

On October 21, 2021, **Kintor Pharmaceutical Limited announced** that the clinical trial of GT90008 for the treatment of advanced solid tumors was approved by China's National Medical Products Administration on October 21, 2021. Kintor Pharma obtained an exclusive license in Greater China for GT90008 from US-based company Gensun in August 2020.

• GT90008 is a PD-L1/TGF- $\beta$  dual targeting antibody.

#### First-in-human clinical studies of targeted therapeutics started

On October 18, 2021, **Dragonfly Therapeutics announced** that the first patients were dosed in Phase 1 clinical trials of both the CC-96191 and CC-92328 investigational immunotherapies, which are licensed to Bristol Myers Squibb. The Phase 1 clinical trial (NCT04789655) for the CC-96191 TriNKET and the Phase 1 clinical trial (NCT04975399) for the CC-92328 TriNKET are first-in-human studies that will explore the safety, tolerability and preliminary biological and clinical activity of the respective TriNKET as a single-agent in the setting of relapsed or refractory acute myeloid leukemia.

• TriNKETs are trispecific antibodies that direct endogenous NK cells toward tumor cells. They target two distinct activating receptors on NK cells, plus a tumor antigen.

On October 26, 2021, details were posted on clinical trials.gov for a Phase 1-2 study (**NCT05094804**) of OR2805 alone and in combination with a PD-1 inhibitor in patient with advanced malignancies. Sponsored by OncoResponse, Inc., the study will enroll an estimated 130 patients and has an estimated primary completion date of April 2024.

• OR2805 is an anti-CD163 IgG1 monoclonal antibody.

On October 28, 2021, details were posted on clinical trials.gov for a Phase 1 study (**NCT05098405**) first-in-human, multicenter, open-label, dose-escalation study to characterize the safety and tolerability of MP0317 in patients with relapsed/refractory advanced solid tumors. Sponsored by Molecular Partners AG, the study will enroll an estimated 45 patients and has an estimated primary completion date of March 2024.

• MP0317 is a tri-specific fibroblast activation protein x CD40 DARPin® drug candidate

#### HLX22 (AC101) enters Phase 2 clinical study

On October 20, 2021, **Alligator Bioscience AB announced** that the company was notified that the first patient has been dosed in its Phase 2 clinical trial collaboration with Shanghai Henlius Biotech, Inc. and AbClon, Inc. Alligator out-licensed AC101 to AbClon, Inc. in October 2016. Abclon, Inc. subsequently sub-licensed AC101 in China for clinical development by Shanghai Henlius Biotech Inc. The Phase 2 NCT04908813 study will evaluate HLX22 in combination with trastuzumab and chemotherapy (XELOX) versus placebo in combination with trastuzumab and chemotherapy (XELOX) for treatment of locally advanced or metastatic gastric cancer.

• HLX22 is a humanized anti-HER2 monoclonal antibody.

#### Updates provided on BLAs for bimekizumab and balstilimab

On October 16, 2021, **UCB provided an update** on the U.S. Food and Drug Administration's (FDA) review of the biologics license application (BLA) for bimekizumab. FDA informed UCB that the Agency was unable to complete the review of the BLA for bimekizumab by the PDUFA date and is deferring action on the application because of the inability to conduct onsite facility inspections due to travel restrictions. On August 20, 2021, the European Commission (EC) authorized marketing of Bimzelx (bimekizumab) in the EU for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

 Bimekizumab is a humanized IgG1 antibody that selectively inhibits IL-17A and IL-17F by binding regions that are common to these pro-inflammatory cytokines, which share ~50% sequence identity.

On October 22, 2021, **Agenus announced** a strategic decision to withdraw its BLA for balstilimab monotherapy for the treatment of recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. Following the full approval of pembrolizumab for the treatment of persistent, recurrent, or metastatic cervical cancer on October 13 2021, the FDA no longer considered it appropriate to review balstilimab's BLA for accelerated approval and recommended Agenus withdraw. The decision to withdraw the BLA does not change the development plans for balstilimab combinations.

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

#### Marketing applications validated by EMA

On October 29, 2021, Boehringer Ingelheim announced that the company's marketing

authorization application (MAA) for the treatment of flares in generalized pustular psoriasis (GPP), has been validated and is now under evaluation with the European Medicines Agency (EMA). The MAA includes data from the 12-week randomized, placebo-controlled Phase 2 Effisayil-1 trial (NCT03782792). The study evaluated the efficacy, safety, and tolerability of single 900 mg dose of IV administered spesolimab, with the option of a second dose if symptoms persisted on Day 8 in 53 patients experiencing a GPP flare. The superiority of treatment with spesolimab over placebo in pustular clearance after one week of treatment was demonstrated in the Effisayil-1 trial.

• Spesolimab is a humanized IgG1 antibody that blocks the activation of the interleukin-36 receptor.

On October 29, 2021, **ADC Therapeutics SA announced** its MAA for loncastuximab tesirine (ZYNLONTA®) for the treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL), has been validated by the EMA. In September 2021, the EC granted Orphan Drug designation to ZYNLONTA for the treatment of DLBCL. ZYNLONTA was granted an accelerated approval by the FDA in April 2021 as a single-agent treatment for adult patients with relapsed or refractory DLBCL after two or more lines of systemic therapy.

• Loncastuximab tesirine is a CD19-targeted antibody-drug conjugate.

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### **COVID-19 intervention news**

#### Anti-SARS-CoV-2 antibody therapeutics Ronapreve and Regkirona approved in EU

On November 11, 2021, the European Medicines Agency (EMA)'s human medicines committee recommended authorizing anti-SARS-CoV-2 antibody therapeutics Ronapreve (casirivimab/imdevimab) and Regkirona (regdanvimab) for COVID-19.

• The Committee recommended authorizing Ronapreve for treating COVID-19 in adults and adolescents (from 12 years of age and weighing at least 40 kilograms) who do not require supplemental oxygen and who are at increased risk of their

disease becoming severe. Ronapreve can also be used for preventing COVID-19 in people aged 12 years and older weighing at least 40 kilograms. The company that applied for authorization of Ronapreve was Roche Registration GmbH.

 The Committee recommended authorizing Regkirona for treating adults with COVID-19 who do not require supplemental oxygen and who are also at increased risk of their disease becoming severe. The applicant for Regkirona was Celltrion Healthcare Hungary Kft.

#### On November 12, 2021, the European Commission approved both products.

### **Updates on non-COVID-19 interventions**

#### IgM antibodies the focus of discovery efforts

On November 1, 2021, **AlivaMab Discovery Services (ADS) announced** an expanded agreement with IGM Biosciences. ADS will rapidly discover diverse panels of human antibodies for the development of engineered antibody-based therapeutics by IGM. The multi-target agreement occurs after the successful conclusion of a pilot project in which ADS identified and delivered to IGM a panel of combinatorially diverse, potently functional, high-affinity antibodies in less than three months.

 IGM Biosciences is a clinical-stage company. Their IgM antibodies IGM-2323 and IGM-8444 are being evaluated in Phase 1 studies as treatments for cancer. IGM-2323 is a bispecific antibody targeting CD20 and CD3, IGM-8444 is a monospecific antibody targeting DR5.

#### Plans announced for first in human clinical studies in 2021-2

On November 4, 2021, IgM Biosciences announced plans to advance 3 IgM antibodies into clinical studies.

- IGM-6268 is an IgM version of an anti-SARS-CoV-2 IgG monoclonal antibody and is being developed as an intranasally
  administered agent for the treatment and prevention of COVID-19. It is expected to start clinical development by the end
  of 2021, initially in healthy volunteers.
- IGM-7354 is an IL-15 x PD-L1 bispecific IgM antibody. A clinical study in solid tumors is planned for 2022.
- IGM-2644 is a CD38 x CD3 bispecific IgM antibody. A clinical study in multiple myeloma is planned for 2022.

On November 4, 2021, **Prothena Corporation plc announced** that they presented preclinical results at the Alzheimer's Association International Conference® 2021 demonstrating that PRX012 significantly cleared both pyroglutamate-modified and - unmodified amyloid beta plaque in post-mortem brain tissue of late-stage Alzheimer's disease patients. The company plans to submit an Investigational New Drug Application in 1Q 2022.

• PRX012 is a monoclonal antibody targeting a key epitope at the N-terminus of amyloid beta.

#### New antibody therapeutic queued for clinical study

On November 1, 2021, details were posted on clinical trials.gov for a Phase 1/2 study (**NCT05102214**) of HXL301 in patients with locally advanced or metastatic solid tumors. Sponsored by Shanghai Henlius Biotech, the study will enroll an estimated 150 patients and has estimated dates for initiation in January 2022 and primary completion in March 2023.

• HXL301 is a recombinant humanized anti-PDL1 and anti-TIGIT bispecific antibody.

On November 2, 2021, details were posted on clinical trials.gov for a Phase 1 first-in-human, dose-escalation study (**NCT05103683**) of TORL-1-23 in participants with advanced cancer. Sponsored by TORL Biotherapeutics, LLC, the study will enroll an estimated 70 patients and has estimated dates for initiation in November 2021 and primary completion in November 2024.

• TORL-1-23 is an antibody-drug conjugate targeting an undisclosed antigen.

On November 11, 2021, details were posted on clinical trials.gov for a Phase 1 study (**NCT05116709**) to evaluate the safety, tolerability, pharmacokinetic characteristics and preliminary clinical efficacy of BAT6005 in patients with advanced malignant solid tumors. Sponsored by Bio-Thera Solutions, the study will enroll an estimated 36 patients and has estimated dates for initiation in November 2021 and primary completion in December 2022.

• BAT6005 is a monoclonal antibody that targets TIGIT.

#### First in human studies started

On November 1, 2021, details were posted on clinical trials.gov for a Phase 1 study (**NCT05102136**) that is evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of single ascending doses of REGN9933. Sponsored by Regeneron, the study will enroll an estimated 72 patients and has an estimated primary completion date in November 2022.

• REGN9933 is an anti-Factor XI monoclonal antibody.

On November 10, 2021, details were posted on clinical trials.gov for a Phase 1 study (**NCT05114889**) to evaluate safety and tolerability of BSI-045B in healthy adult subjects and patients with atopic dermatitis. Sponsored by Biosion, Inc., the study will enroll an estimated 68 patients and has an estimated primary completion date in November 2022.

• BSI-045B is anti-thymic stromal lymphopoietin monoclonal antibody.

#### Global clinical development of tanezumab terminated

On November 2, 2021, **Pfizer announced** the discontinuation of the global clinical development program of tanezumab following receipt of a Complete Response letter from the US Food and Drug Administration (FDA) for tanezumab's biologics license application (BLA) for osteoarthritis pain and a negative opinion adopted by the EMA on tanezumab's marketing authorization application in osteoarthritis pain.

• Tanezumab (PF-04383119, Raylumis) is a humanized IgG2 antibody targeting nerve growth factor developed by Pfizer and Eli Lilly and Company as a treatment of pain.

#### FDA accepts BLA for toripalimab

On November 1, 2021, **Coherus BioSciences**, Inc. and Shanghai Junshi Biosciences Co., Ltd. announced that the FDA accepted for review the BLA for toripalimab in combination with gemcitabine and cisplatin for the first-line treatment for patients with advanced recurrent or metastatic nasopharyngeal carcinoma and toripalimab monotherapy for the second-line or above treatment of recurrent or metastatic NPC after platinum-containing chemotherapy. The FDA has granted a Priority Review for the toripalimab BLA and set a first action date for April 2022.

• Toripalimab is a humanized anti-PD-1 IgG4 monoclonal antibody with a S228P hinge mutation.

#### NMPA accepts NDA for socazolimab

On November 1, 2021, **Sorrento Therapeutics, Inc. announced** that its license partner, China Oncology Focus Limited (COF), an affiliate of Lee's Pharmaceutical Holdings Limited, has submitted a new drug application for socazolimab, licensed from Sorrento to COF for the greater China territory to treat recurrent or metastatic cervical cancer. The NDA application has been accepted by China National Medical Products Administration.

• Socazolimab is a human anti-PD-L1 monoclonal antibody.

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### **COVID-19 intervention news**

#### New company developing anti-SARS-CoV-2 antibody launched

On November 15, 2021, **Twist Bioscience Corporation announced** it has launched Revelar Biotherapeutics, Inc., an independently operated, new biotechnology company to develop and commercialize an antibody, discovered and optimized by Twist Biopharma, a division of Twist Bioscience, that neutralizes all known variants of concern of the SARS-CoV-2 virus in preclinical studies. The antibody will enter clinical studies in 2022, pending completion of necessary requirements.

#### New anti-SARS-CoV-2 antibodies queueing for clinical study

On November 22, 2021, PRNewswire reported that **SYZJ001**, an antibody-based drug for **COVID-19** jointly developed by Shanghai ZJ Bio-Tech Co., Ltd. and Sanyou Biopharmaceuticals (Shanghai) Co., Ltd., was discussed during the opening ceremony of the 4th China International Import Expo held in Shanghai on November 6, 2021. Boehringer-Ingelheim is in charge of process optimization and manufacturing services. The project has formally entered the pre-Investigational New Drug (pre-IND) procedure for application of Phase 1 clinical trials in China and the US.

 SYZJ001 is composed of a human IgG antibody and a humanized single domain antibody targeting the receptor binding domain (RBD) of SARS-CoV-2's Spike protein. The two antibodies can non-competitively bind to the antigenic epitopes of RBD proteins, block the binding between the virus and human ACE2 receptors, and efficiently neutralize SARS-CoV-2 and prevent cell infection.

On November 29, 2021, **Immunome, Inc. announced** that it has submitted an IND application to the U.S. Food and Drug Administration (FDA) for IMM-BCP-01 for the treatment of SARS-CoV-2 (COVID-19). Immunome plans to initiate a placebo-controlled dose escalation study of IMM-BCP-01 in patients infected with SARS-CoV-2, pending FDA's acceptance of Immunome's IND submission.

• IMM-BCP-01 is a three-antibody cocktail targeting non-overlapping regions of the Spike protein and elicits multi-modal activity in pre-clinical testing.

#### Nebulized formulation of antibody cocktail in development

On November 29, 2021, **Celltrion Group announced** that the company has accelerated development of a nebulized formulation of its neutralizing antibody cocktail treatment to respond to emerging mutants from SARS-CoV-2. The antibody cocktail consists of CT-P63 together with Regkirona (regdanvimab, CT-P59), which was recently approved by the European Commission for the treatment of COVID-19. Celltrion enrolled 24 healthy volunteers in its global Phase I clinical trial to evaluate the safety, tolerability and pharmacokinetics of CT-P63 and the company anticipates results by the end of the year.

• CT-P63 and Regkirona are monoclonal antibodies that target the SARS-CoV-2 spike RBD.



### Updates on non-COVID-19 interventions

#### New antibodies queueing for clinical study

On November 15, 2021, LAVA Therapeutics N.V. reported that plans are on track to initiate the

company's Phase 1/2a clinical trial of LAVA-1207 in patients with metastatic castration-resistant prostate cancer (mCRPC) later in Q4 2021. The open-label, multi-center, Phase 1/2a clinical trial will evaluate safety, tolerability, pharmacokinetics, pharmacodynamics, immunogenicity and preliminary antitumor activity of LAVA-1207 in patients with mCRPC.

• LAVA-1207 is a bispecific gamma delta T cell engager (Gammabody<sup>™</sup>) that targets the prostate-specific membrane antigen and has demonstrated preclinical proof-of-concept in a variety of preclinical models to support acceptance of a CTA/IND to study in humans.

On November 18, 2021, details were posted on clinical trials.gov for a Phase 1/2 study (**NCT05125016**) of REGN4336 administered alone or in combination with cemiplimab in patients with mCRPC. Sponsored by Regeneron Pharmaceuticals, the study will enroll an estimated 199 patients and has estimated dates for initiation in November 2021 and primary completion in August 2026.

• REGN4336 is a bispecific T-cell engaging antibody that targets PSMA and CD3.

On November 22, 2021, details were posted on clinical trials.gov for a randomized, double-blind, placebo-controlled, Phase 1 single ascending dose study (**NCT05128409**) to evaluate the safety, tolerability, and pharmacokinetics of XKH001 injection in healthy adults. Sponsored by Beijing Kanova Biopharmaceutical Co., Ltd., the study will enroll an estimated 35 patients and has estimated dates for initiation in January 2022 and primary completion in July 2022.

• XKH001 is an IgG1 antibody that targets IL-25 (also known as IL-17E).

#### New antibody-drug conjugate enters a first-in-human study

On November 17, 2021, details were posted on clinical trials.gov for a Phase 1/2a multi-center, open-label master protocol (**NCT05123482**) to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary antitumor activity of AZD8205 in participants with advanced or metastatic solid malignancies. Sponsored by AstraZeneca, the study will enroll an estimated 186 patients and has a primary completion date in May 2025.

• AZD8205 is an antibody-drug conjugate that has the potential to treat a wide variety of solid tumors; limited information about the molecule is available as of December 1, 2021.

On November 30, 2021, **TG Therapeutics, Inc. announced** the FDA notified the company that it plans to host a meeting of the Oncologic Drugs Advisory Committee in connection with its

review of the pending Biologics License Application (BLA)/supplemental New Drug Application (sNDA) for the combination of ublituximab and UKONIQ® (umbralisib) for the treatment of adult patients with chronic lymphocytic leukemia and small lymphocytic lymphoma. The date of the meeting has not yet been determined, but it may occur in March or April 2022. Given this timing, the company believes it is unlikely that the FDA will make a decision on the BLA/sNDA by March 25, 2022, which is the FDA's goal date for a first action on the application.

• Ublituximab is a chimeric anti-CD20 IgG1k antibody with low fucose content in its Fc region, which enhances its effector functions.

#### Envafolimab approved in China for treatment of solid tumors

On November 29, 2021, **TRACON Pharmaceuticals reported** that its partners Alphamab Oncology and 3D Medicines (Beijing) Co., Ltd. announced that envafolimab (KN035), an PD-L1 antibody formulated for subcutaneous injection, received marketing authorization from the Chinese National Medical Products Administration. Envafolimab was approved for adult patients with microsatellite instability-high or deficient mismatch repair advanced solid tumors based on data from a pivotal Phase 2 study.

• Envafolimab is composed of an anti-PD-L1 single domain antibody fused with an Fc.

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Antibody Engineering & Therapeutics, December 12-16, 2021

December 1 - 15, 2021

### **COVID-19 intervention news**

#### Memo Therapeutics AG aims to start clinical studies of COVAB 36

On December 13, 2021, **Memo Therapeutics AG announced** the receipt of CHF 10.5 million from the Swiss Federal Funding Programme for COVID-19 Medicines to clinically develop COVAB 36 for the treatment of SARS-CoV-2 infections. COVAB 36 can be administered via inhalation, which could enhance patient acceptance. The project also includes the ability to rapidly develop a combination antibody partner for COVAB 36 targeted against emerging variants through an ultra-fast update process based on Memo Therapeutic AG's antibody discovery platform. The company plans to start Phase 1 clinical studies with COVAB 36 in Q1 2022.

• COVAB 36 is a potent, human anti-SARS-CoV-2 monoclonal antibody.

#### SCTA01C and SCTA01 combo to be evaluated in Phase 1/2/3 study

On December 14, 2021, details were posted on clinical trials.gov for an adaptive Phase 1/2/3 study (**NCT05156645**) to evaluate the efficacy and safety of the SCTA01C and SCTA01 combination for treatment of outpatients with COVID-19. Sponsored by Sinocelltech Ltd., the study will enroll an estimated 343 patients and has estimated dates for initiation in January 2022 and primary completion in December 2022.

 SCTA01C and SCTA01 are anti-SARS-CoV-2 antibodies that target different epitopes of the viral spike protein.

#### Phase 2/3 study of ADM03820 to start soon

On December 2, 2021, details were posted on clinical trials.gov for a randomized, double-blind, placebo-controlled, multi-center Phase 2/3 study (**NCT05142527**) study to evaluate the safety, tolerability, and efficacy of ADM03820 to prevent symptomatic COVID-19 in adult subjects. Sponsored by Ology Bioservices, the study will enroll an estimated 4450 patients and has estimated dates for initiation in December 2021 and primary completion in April 2023.

• ADM03820 is a 1:1 mixture of two human IgG1 non-competitive binding anti-SARS-CoV-2 antibodies.

#### Actemra®/RoActemra® approved for COVID-19 in Australia and the EU

On December 1, 2021, the Australian Therapeutic Goods Administration granted provisional approval to Roche Products Pty Ltd for the use of tocilizumab (ACTEMRA) for the treatment of COVID-19. The provisional approval is for the intravenous treatment of confirmed COVID-19 in hospitalized adults aged 18 years and older who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. On December 7, 2021, Roche announced that the European Commission has extended the marketing authorization for Actemra®/RoActemra® (tocilizumab) to include the treatment of COVID-19 in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. This decision comes just hours after the recommendation by the European Medicines Agency's Committee for Medicinal Products for Human Use, reflecting the urgent need for the product as a potential treatment option during the COVID-19 public health emergency.

• Tocilizumab is an anti-IL-6 receptor monoclonal antibody previously approved for the treatment of adult patients with moderate-to-severe active rheumatoid arthritis.

#### Evusheld receives emergency use authorization in the US

On December 8, 2021, the U.S. Food and Drug Administration (FDA) issued an emergency use authorization for AstraZeneca's Evusheld (tixagevimab co-packaged with cilgavimab and administered together) for the pre-exposure prophylaxis (prevention) of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kilograms [about 88 pounds]).

 Evusheld, comprising the combination of 2 human anti-SARS-CoV-2 IgG1k antibodies, was derived from B cells from convalescent patients after infection with SARS-CoV-2. Discovered by Vanderbilt University Medical Center, the antibodies bind to distinct sites on the SARS-CoV-2 spike protein. These antibodies were licensed to AstraZeneca in June 2020, and then engineered with mutations that extend half-life (YTE) and reduce Fc receptor and complement C1q binding (L234F, L235E, P331S).

#### Amubarvimab/romlusevimab combination approved in China

On December 9, 2021, Brii Biosciences Limited announced that the National Medical

Products Administration (NMPA) of China has granted approval of the amubarvimab/romlusevimab combination (previously BRII-196/BRII-198 combination), for the treatment in adults and pediatric patients (age 12-17 weighing at least 40 kg) with mild and normal type of COVID-19 at high risk for progression to severe disease, including hospitalization or death. The indication of pediatric patients (age 12-17 weighing at least 40 kg) is under a conditional approval. Brii Bio is also seeking U.S. FDA Emergency Use Authorization for the amubarvimab/romlusevimab combination.

 Amubarvimab and romlusevimab are non-competing SARS-CoV-2 monoclonal neutralizing antibodies derived from convalesced COVID-19 patients developed in collaboration with the 3rd People's Hospital of Shenzhen and Tsinghua University.



### Updates on non-COVID-19 interventions

#### IND for GSK4381562 cleared by FDA

On December 1, 2021, **Surface Oncology announced** that the FDA has cleared the Investigational New Drug Application for GSK4381562 (formerly SRF813) to proceed into a first-in-human clinical trial. The company had announced in December 2020 that it entered into an agreement in which GlaxoSmithKline exclusively licensed worldwide development and commercial rights to GSK4381562.

• GSK4381562 is a human, IgG1 antibody targeting PVRIG (also known as CD112R), an inhibitory protein expressed on natural killer cells (NK cells) and T cells.

#### Clinical Trial Application submitted for BI-1607

On December 8, 2021, **BioInvent International AB announced** it has submitted a Clinical Trial Application for a Phase 1/2 study of its novel FcyRIIB-blocking antibody, BI-1607. BioInvent intends to explore the activity of BI-1607 in advanced solid tumors and antibody combinations supported by strong preclinical data.

• BI-1607 is a human monoclonal antibody that targets FcyRIIB. Its Fc region has been modified to alter its affinity for Fc receptors.

#### Bristol Myers Squibb licenses Immatics' TCR bispecific program IMA401

On December 14, 2021, **Immatics N.V. and Bristol Myers Squibb announced** that they have entered into a license, development and commercialization agreement for Immatics' T cell receptor bispecific candidate, IMA401. Immatics retains the options to co-fund U.S. development in exchange for enhanced U.S. royalty payments and/or to co-promote IMA401 in the US. In November 2021, Immatics filed a Clinical Trial Application with Paul-Ehrlich-Institute, the German federal regulatory authority, for the development of IMA401. The clinical trial, which is planned to commence in the first half of 2022, will enroll patients across various solid tumor types.

 IMA401 is a half-life extended TCER® molecule that targets an HLA-A\*02-presented (human leukocyte antigen) peptide derived from two different cancer-associated proteins, melanoma-associated antigen 4 and/or 8.

#### First Phase 1 studies due to start

On December 6, 2021, details were posted on clinical trials.gov for a Phase 1 study multicenter, open-label, first-in-human clinical trial (**NCT05145179**) to evaluate the safety, tolerability, pharmacokinetics and potential anti-tumor effects of SSGJ-705 in patients with advanced or metastatic her2-expressing solid tumors. Sponsored by the Sunshine Guojian Pharmaceutical (Shanghai) Co., Ltd., the study will enroll an estimated 162 patients and has estimated dates for initiation in December 2021 and primary completion in December 2023.

 SSGJ-705 is a recombinant anti-HER2 x anti-PD-1 bispecific antibody constructed by fusing scFvs (anti-PD1) with the effector-functional Fc of an IgG (trastuzumab) via a flexible peptide linker.

On December 9, 2021, details were posted on clinical trials.gov for a Phase 1 study (**NCT05150457**) to evaluate the safety, tolerability, pharmacokinetics, and preliminary efficacy of BNA035 in patients with advanced solid tumors. Sponsored by Binacea Pharma, Inc., the study will enroll an estimated 48 patients and has estimated dates for initiation in January 2022 and primary completion in November 2023.

 BNA035 is an anti-epidermal growth factor receptor (EGFR) x anti-CD137 bispecific antibody.

On December 14, 2021, details were posted on clinical trials.gov for a Phase 1 study (**NCT05156866**) of TORL-2-307-ADC in participants with advanced cancer. Sponsored by TORL Biotherapeutics, LLC, the study will enroll an estimated 70 patients and has estimated dates for initiation in January 2022 and primary completion in January 2025.

• TORL-2-307-ADC is an antibody-drug conjugate targeting an undisclosed antigen.

#### Amivantamab approved in the European Union

On December 10, 2021, The Janssen Pharmaceutical Companies of Johnson & Johnson announced Conditional Marketing Authorisation of RYBREVANT® (amivantamab) for the treatment of adult patients with advanced NSCLC with activating epidermal growth factor receptor (EGFR) exon 20 insertion mutations, after failure of platinum-based therapy. Amivantamab is the first approved treatment in the European Union specifically targeting EGFR exon 20 insertion mutations for NSCLC.

 Amivantamab is a human anti-EGFR x anti-MET bispecific antibody derived from Genmab's DuoBody technology platform.

December 15, 2021 - January 1, 2022

# We wish you a happy, healthy & prosperous 2022!

### **COVID-19 intervention news**

#### Phase 1 study of anti-SARS-CoV-2 antibody cocktail to start

On December 17, 2021, details were posted on clinicaltrials.gov for a Phase 1 study (**NCT05162365**) of the safety, tolerability, and efficacy of IBI314 in ambulatory patients with COVID-19. Sponsored by Innovent Biologics, study will enroll an estimated 240 patients and has an estimated primary completion date in July 2022.

• IBI314 is a cocktail of two anti-SARS-CoV-2 Spike protein IgG1 antibodies, IBI314-A and IBI314-B, in a 1:1 [w/w] ratio.

#### Phase 1 study of IgM antibody started

On December 16, 2021, details were posted on clinicaltrials.gov for a Phase 1 study (NCT05160402) evaluating the safety, tolerability, and pharmacokinetics of intranasal plus intraoral IGM-6268 in healthy volunteers. In this 6-arm study, IGM-6268 (1 mg, 3.75 mg, 7.5 mg) or placebo will be administered by intranasal + intraoral spray using a Teleflex Mucosal Atomization Device Nasal™ Intranasal Mucosal Atomization Device once, or once or twice each day for 5 days. Sponsored by IGM Biosciences, Inc., the study will enroll an estimated 48 patients and has an estimated primary completion date in March 2022.

 IGM-6268 is an engineered Immunoglobulin M (IgM) antibody that specifically targets the receptor binding domain of the SARS-CoV-2 spike protein. This humanized pentameric IgM antibody has 10 binding sites to the spike protein and a J-chain to enable the formation of IgM pentamers.

#### Xevudy (sotrovimab) approved in the EU

On December 17, 2021, **GlaxoSmithKline plc and Vir Biotechnology, Inc. announced** the marketing authorization for Xevudy (sotrovimab) for the early treatment of COVID-19 in the European Union. Sotrovimab is now approved there for the treatment of adults and adolescents (aged 12 years and over and weighing at least 40kg) with COVID-19 who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19.

Sotrovimab is a human anti-SARS-CoV-2 antibody incorporating Xencor, Inc.'s Xtend<sup>™</sup> technology that has been designed to achieve high concentration in the lungs to ensure optimal penetration into airway tissues affected by SARS-CoV-2 and to have an extended half-life.



### **Updates on non-COVID-19 interventions**

#### IND for DS-7011 filed

During **R&D Day 2021 presentations on December 14-15, 2021**, Daiichi Sankyo revealed that they filed an investigational new drug application for DS-7011. The target indication is systemic lupus erythematosus, and a Phase 1 study is planned for January 2022.

• DS-7011 is an anti-toll-like receptor 7 antibody.

#### First Phase 1 study started

On December 17, 2021, details were posted on clinicaltrials.gov for a Phase 1a/1b, trial (**NCT05162755**) investigating the safety, tolerability, and preliminary anti-neoplastic activity of S095029 as monotherapy and in combination with Sym021 in patients with advanced solid tumor malignancies followed by an expansion part with triplet combinations of S095029 and Sym021 and futuximab/modotuximab in patients with metastatic gastric or colorectal cancers. Sponsored by Institut de Recherches Internationales Servier, the study will enroll an estimated 119 patients and has an estimate primary completion date in May 2023.

• S095029 is an anti-NKG2A antibody, Sym021 is an anti-PD-1 antibody, and futuximab and modotuximab are monoclonal antibodies that target HER2 and EGFR, respectively.

#### Biologic license applications submitted to FDA

On December 15, 2021, **Boehringer Ingelheim announced** that the U.S. Food and Drug Administration (FDA) has accepted a Biologics License Application (BLA) and granted Priority Review for spesolimab for the treatment of generalized pustular psoriasis (GPP) flares. Spesolimab has been granted US Orphan Drug Designation for the treatment of GPP, and Breakthrough Therapy Designation for the treatment of GPP flares in adults.

• Spesolimab is a humanized anti-interleukin 36 receptor IgG1 antibody with Fc mutations (L234A/L235A) that remove effector function.

On December 29, 2021, The Janssen Pharmaceutical Companies of Johnson & Johnson announced the submission of a BLA to the FDA seeking approval of teclistamab for the treatment of patients with relapsed or refractory (R/R) multiple myeloma. The BLA submission for teclistamab is supported by data from MajesTEC-1 (NCT04557098, NCT03145181), an open-label, multicenter clinical trial evaluating the safety and efficacy of teclistamab in adults with R/R multiple myeloma. Data from this study were recently reported at the 2021 American Society of Hematology annual meeting.

• Teclistamab is a T-cell redirecting, bispecific antibody targeting B-cell maturation antigen and CD3.

#### Aducanumab receives a negative opinion in the EU

On December 17, 2021, **Biogen announced** that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency has adopted a negative opinion on the Marketing Authorization Application for aducanumab for the treatment of mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease dementia. Biogen will seek a re-examination of the opinion by the CHMP. In June 2021, the FDA granted accelerated approval for ADUHELM® (aducanumab-avwa) 100 mg/mL injection for intravenous use as an Alzheimer's disease treatment.

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

#### Sugemalimab approved in China

On December 21, 2021, **CStone Pharmaceuticals announced the approval in China of Cejemly® (sugemalimab)** in combination with pemetrexed and carboplatin as first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations; and in combination with paclitaxel and carboplatin as first-line treatment of patients with metastatic squamous NSCLC. The approval is based on the results of the Phase 3 GEMSTONE-302 study in which, compared with placebo plus chemotherapy, Cejemly® plus chemotherapy lowered the risk of disease progression or death by 52%, significantly prolonged the patients' progression-free survival and an encouraging trend in overall survival was observed.

• Sugemalimab is an anti-PD-L1 monoclonal antibody.

#### Three antibody-based products approved by FDA

On December 17, 2021, **FDA approved VYVGARTô (efgartigimod alfa-fcab)** for the treatment of generalized myasthenia gravis in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. The approval of VYVGART is based on results from the global Phase 3 ADAPT trial, which were **published in the July 2021 issue of The Lancet Neurology.** In this study, 68% of AChR antibody positive gMG patients treated with VYVGART were responders (n=44/65) on the Myasthenia Gravis - Activities of Daily Living (MG-ADL) scale compared with 30% of patients treated with placebo (n=19/64) (p<0.0001) during the first treatment cycle.

• VYVGART is a human IgG1 antibody fragment that binds to FcRn, resulting in the reduction of circulating IgG antibodies.

On December 17, 2021, Amgen announced FDA's approval of Tezspire<sup>™</sup> (tezepelumabekko) for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma. The approval was based in part on results from the pivotal NAVIGATOR Phase 3 trial in which Tezspire demonstrated superiority across every primary and key secondary endpoint in patients with severe asthma, compared to placebo, when added to standard therapy. Marketing applications for Tezspire are under regulatory review in the European Union, Japan and other countries.

• Tezepelumab is a human monoclonal antibody targeting thymic stromal lymphopoietin.

On December 28, 2021, LEO Pharma A/S announced that the FDA approved Adbry<sup>™</sup> (tralokinumab) for the treatment of moderate-to-severe atopic dermatitis in adults 18 years or older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Tralokinumab had previously been approved in the European Union, in June 2021, for the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy. The approvals were supported by data from two Phase 3 monotherapy efficacy and safety studies (ECZTRA 1 (NCT03131648) and ECZTRA 2 (NCT03160885)), as well as a Phase 3 combination therapy efficacy and safety study (ECZTRA 3 (NCT03363854)).

• Tralokinumab is a human IgG4 antibody that interferes with IL-13-mediated signaling by blocking its interactions with both IL-13 receptor α1 and IL-13 receptor α2.

### Attending a meeting soon?

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

**PepTalk**, January 17-19, 2022

• Use code TAS20 for a 20% discount