Antibody News You Should Know

January 1 to 15, 2020

Antibody-based therapeutics are advancing in clinical development at a rapid rate and being approved in record numbers. Recent news about antibody-related events are summarized below. Follow the links for more details.

Antibodies in preclinical development

On January 6, 2020 Yisheng Biopharma Co., Ltd. and Tavotek Biotherapeutics announced that the companies have entered into a strategic research alliance and collaborate in the development involving their lead assets in oncology. The objective of the alliance is to co-develop a combination therapy including Tavo-201/203 for cancer treatment.

- Tavo-201/203 is a series of novel multi-specific human antibody-based immuno-oncology assets developed using Tavotek's proprietary TavoSelect Platform.

On January 9, 2020 Boehringer Ingelheim announced the acquisition of worldwide exclusive rights to Enleofen Bio Pte. Ltd.'s preclinical interleukin-11 (IL-11) platform. This acquisition will enable Boehringer Ingelheim to develop first-in-class therapies across a broad range of fibro-inflammatory diseases

such as non-alcoholic steatohepatitis and interstitial lung diseases. Since its founding in 2017, Enleofen has built an extensive anti-IL-11 antibody platform and advanced molecules towards the clinic, including Enx108A.

- Enx108A is a human antibody that targets IL-11.

Phase 1 studies planned or started

On On January 8, 2020 Inhibrx, Inc. announced the administration of the first dose of INBRX-106 in a Phase 1 dose-escalation clinical study (NCT04198766) of patients with locally advanced or metastatic solid tumors. The ongoing clinical study aims to determine the safety of INBRX-106 as a single agent and in combination with the anti-PD-1 checkpoint inhibitor pembrolizumab (Keytruda), as well as the recommended therapeutic dose level for future clinical development.

- INBRX-106 is a hexavalent agonist of OX40, a co-stimulatory receptor expressed on immune cells.

The estimated study start date for NCT04221542, a Phase 1 study evaluating the safety, tolerability, pharmacokinetics, and efficacy of AMG 509 in subjects with metastatic castration-resistant prostate cancer, is January 10, 2020. The dose exploration phase of the study will estimate the maximum tolerated dose (MTD) of AMG 509 using a Bayesian logistic regression model. The recommended Phase 2 dose may be identified based on emerging safety, efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) data prior to reaching an MTD. Alternative dosing schedule(s) may be explored based on emerging safety and PK data.

- AMG509 is a bispecific antibody targeting STEAP-1 and CD3.

The estimated study start date for the DS-2741a Phase 1 study is January 13, 2020. NCT04211415 is a three-part first-in-human study of single ascending dose and multiple doses to assess the safety, PK and PD of DS-2741a after subcutaneous injection in healthy Japanese male subjects, and single dose study to assess the PK, safety, PD and efficacy of DS-2741a after subcutaneous injection in Japanese subjects with moderate to severe atopic dermatitis.

- DS-2741a is a humanized antibody targeting Orai1, a pore-forming subunit of calcium release-activated calcium (CRAC) channels that is essential for activation of T cells and other immune cells in atopic dermatitis.

Marketing applications planned or submitted

On January 9, 2020 ADC Therapeutics SA announced positive results from the pivotal 145-patient Phase 2 clinical trial of loncastuximab tesirine (ADCT-402) for the treatment of relapsed or refractory diffuse large B-cell lymphoma. The study exceeded its primary endpoint target with 45.5% overall response rate, including 20% complete response rate. The company indicated that they are on track for submission of a biologics license application submission in 3Q 2020.

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

At the JP Morgan Healthcare conference, held January 12-16, 2020, GlaxoSmithKline announced that they **anticipate dostarlimab will be approved** for the treatment of 2nd-line endometrial cancer in 2020.

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

On January 2, 2020 Innate Pharma SA announced that the European Medicines Agency has accepted the marketing authorization application for Lumoxiti® (moxetumomab pasudotox), a first-in-class medicine indicated for adult patients with relapsed or refractory hairy cell leukemia who have received at least two prior systemic therapies, including treatment with a purine nucleoside analog. The U.S. Food and Drug Administration (FDA) approved Lumoxiti for this indication in September 2018.

- Moxetumomab pasudotox is an immunotoxin comprising an anti-CD22 IgG1k variable fragment conjugated to modified PE38.

In other news...

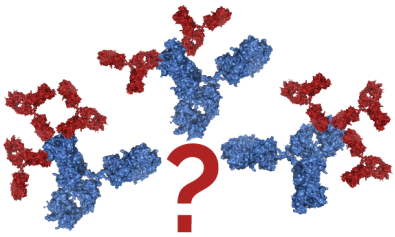
Curis, Inc. announced that it has entered into an option and to acquire ex lusive, worldwide rights from ImmuNext Inc. mercialize anti-VISTA antibodi s for the treatment ng ImmuNext's lead compound, CI-8993 (formerly JNJ-61610 riginally developed as part of a license and collaboration agr uNex t and Janssen Biotech, Inc. In 2016, Janssen initiated a Phase 1 study of CI-8993 evaluating safety, pharmacokinetics and pharmacodynamics of ascending doses of CI-8993 in patients with advanced solid tumors. Of 12 patients enrolled, one experienced dose-limiting side effects related to cytokine release syndrome. Janssen opted to close the study and ImmuNext regained control of the asset.

CI-8993 (onvatilimab) is a human IgG1 antibody targeting VISTA (V-domain Ig Suppressor of T-cell Activation); Curis plans to initiate a Phase 1a/1b study of CI-8993 in 2020.

On January 10, 2020 Eli Lilly and Company and Dermira, Inc. announced a definitive agreement for Lilly to acquire Dermira for approximately $1.1 billion in an all-cash transaction. The acquisition will expand Lilly's immunology pipeline with the addition of lebrikizumab, which is being evaluated in a Phase 3 clinical development program for the treatment of moderate-to-severe atopic dermatitis in adolescent and adult patients, ages 12 years and older. Lebrikizumab was granted Fast Track designation from the FDA in December 2019.

- Lebrikizumab is a humanized IgG4 antibody designed to bind IL-13 with high affinity.

The Antibody Society presents:



Antibody Validation Webinar Series

Visit our Learning Center to register for upcoming and On Demand webinars!

The Antibody Society has invited leaders in antibody research from industry and academia to reflect on antibody validation. They paint a uniformly alarming picture of inadequacies at many levels – which encourages users to be highly aware of the consequences of inadequate tool antibody validation, which threaten their biological endeavors.

Series moderator: Dr. Simon Goodman, Science & Technology Program Manager, The Antibody Society

Upcoming Webinar Broadcast:
Webinar #6: Even the Easy Stuff Isn't

January 22, 2020, 10am Eastern Standard Time / 4pm Central European Time, 30 min. webinar + 15 min. chat

Professors Aldrin Gomes and James Trimmer, both from University of California, Davis, dissect two “basic” validation technologies, Western blot and immunohistochemistry, to expose the very many things that can distort validation data.
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Our mailing address is:
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From: The Antibody Society <membership@antibodysociety.org>
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Antibody News You Should Know

January 15 to February 1, 2020

Antibody-based therapeutics are advancing in clinical development at a rapid rate and being approved in record numbers. Recent news about antibody-related events are summarized below. Follow the links for more details.

Investigational new drug application updates

On January 20, 2020, Transcenta Holding Limited announced that an **investigational new drug (IND) application for TST001** for the treatment of solid tumors, submitted by its Suzhou subsidiary Mabspace Biosciences, has been accepted by the Center for Drug Evaluation (CDE) of the National Medical Products Administration of China. The company expects to file an IND in the US soon.

- TST001 is a humanized monoclonal antibody targeting Claudin 18.2.

On January 27, 2020, Surface Oncology announced the **U.S. Food and Drug Administration (FDA) had cleared the Investigational New Drug (IND) applications for its antibody candidates SRF617 and SRF388**, and the company is executing on plans to initiate clinical trials to advance both programs. The company also announced a strategic restructuring that will

reduce its workforce by approximately 35%.

- SRF617 is a human anti-CD39 antibody designed to promote anti-tumor immunity through a dual mechanism of reducing immunosuppressive adenosine and driving the extracellular accumulation of immunostimulatory ATP within the tumor microenvironment. SRF617 will be evaluated in patients with advanced solid tumors both as a monotherapy and in combination with other cancer therapies.
- SRF388 is a human anti-IL-27 antibody designed to inhibit the activity of this highly immunosuppressive cytokine. Surface Oncology has identified particular tumor types, including hepatocellular and renal cell carcinoma, where IL-27 appears to play an important role in the immunosuppressive tumor microenvironment and may contribute to resistance to treatment with checkpoint inhibitors.

On January 30, 2020, F-star Therapeutics Ltd. announced that the **FDA has cleared its IND application for FS120**. F-star expects to enroll 70 patients in a Phase 1 dose escalation clinical trial to assess the safety, tolerability and efficacy of FS120 in patients with advanced malignancies.

- FS120 is a dual agonist bispecific antibody that targets CD137 (4-1BB) and OX40 (CD134, TNFRSF4), two receptors present on the surface of tumor-infiltrating lymphocytes. The Fc effector functions of FS120 have been silenced.

Phase 1 studies planned or started

A first-in-human, two-part clinical **study (NCT04243499) to assess the safety, tolerability and activity of IV doses of ICT01** as monotherapy and in combination with a checkpoint inhibitor in patients with advanced-stage, relapsed/refractory cancer is scheduled to start in January 2020. First posted on clinicaltrials.gov on January 28, 2020, this study is not yet recruiting patients.

- ICT01 is a humanized monoclonal antibody targeting butyrophilin 3A developed by ImCheck Therapeutics.

A Phase 1/1b open-label, multi-center dose escalation **study (NCT04240704) of JBH492** in patients with relapsed/refractory chronic lymphocytic leukemia and non-Hodgkin's lymphoma is scheduled to start in March 2020. First posted on clinicaltrials.gov on January 27, 2020, this study is not yet recruiting patients.

JBH492 is an anti-CCR7 antibody-drug conjugate developed by Novartis Pharmaceuticals.

A Phase 1, open-label, multiple-ascending dose **study (NCT04242147) to investigate the safety, pharmacokinetics, pharmacodynamics, and preliminary efficacy of KD033** in subjects with metastatic or locally advanced solid tumors is scheduled to start in April 2020. First posted on clinicaltrials.gov on January 27, 2020, this study is not yet recruiting patients.

- KD033 is an anti-PD-L1/IL-15 fusion antibody prepared by combining a human, high affinity anti-human/mouse PD-L1 antibody with human IL-15 cytokine. Developed by Kadmon Corporation, LLC, the antibody includes LALA mutations, which eliminate FcγR binding.

A first-in-human Phase 1b dose escalation **trial (NCT04244552) to investigate the safety, tolerability, pharmacokinetics, and biological activity of ATRC-101** in adults with advanced solid malignancies has started recruiting patients.

- ATRC-101 is an engineered, human IgG1 antibody targeting a tumor-restricted ribonucleoprotein complex developed by Atreca, Inc.

Marketing applications updates

During a Q4 earnings conference call on January 28, 2020, Pfizer announced that it completed a marketing application submission for tanezumab in December 2019. This submission was done in close collaboration with the FDA, and it includes the 2.5 mg dose in moderate-to-severe osteoarthritis patients. A decision on the application may occur by the end of 2020. The **submission was confirmed by development partner Eli Lilly**. Tanezumab is also being evaluated in Phase 3 study of patients with cancer pain due to bone metastasis who are taking background opioid therapy.

- Tanezumab is a humanized IgG2 antibody targeting nerve growth factor. A330S and P331S mutations were introduced to decrease effector functions.

On January 21, 2020, GlaxoSmithKline plc announced that the **FDA granted a priority review for the company's Biologics License Application (BLA) seeking approval of belantamab mafodotin** (GSK2857916) for the treatment of patients with relapsed or refractory multiple myeloma whose prior therapy included an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody. The BLA included data from the pivotal DREAMM-2 study, which were recently **published in The Lancet Oncology**.

- Belantamab mafodotin is composed of an afucosylated, humanized IgG1

antibody targeting B-cell maturation antigen conjugated to monomethyl auristatin F.

Marketing approvals

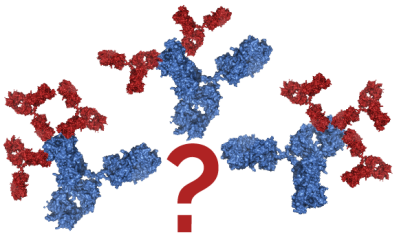
On January 21, 2020, the **FDA approved Tepezza® (teprotumumab-trbw)** for the treatment of adults with thyroid eye disease, which is associated with an outward bulging of the eye that can cause eye pain, double vision, light sensitivity or difficulty closing the eye. Positive data from both **Phase 2 (NCT01868997)** and **Phase 3 (OPTIC, NCT03298867)** studies were reported by Horizon Pharma. In the randomized, placebo-controlled OPTIC study, teprotumumab met the study's primary endpoint, which was a responder rate of ≥ 2 mm reduction of proptosis (bulging) in the study eye (without deterioration in the fellow eye) at Week 24. Data from the OPTIC study showed that 82.9% of patients receiving teprotumumab were proptosis responders compared to 9.5% of patients receiving placebo at Week 24 ($p<0.001$). All secondary endpoints in the study were also met.

- Teprotumumab, a human IgG1 antibody targeting insulin growth factor 1 receptor, was granted Fast Track, Breakthrough Therapy and Orphan Drug designations by the FDA.

On January 21, 2020, Roche announced that the **European Commission granted conditional marketing authorization for polatuzumab vedotin** (Polivy®), in combination with bendamustine plus rituximab (BR), for the treatment of adult patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) who are not candidates for a hematopoietic stem cell transplant. In June 2019, FDA granted accelerated approval for the use of Polivy (polatuzumab vedotin-piiq) in combination with BR for the treatment of people with R/R DLBCL who have received at least two prior therapies.

- Polatuzumab vedotin is a humanized anti-CD79b IgG1 antibody conjugated to monomethyl auristatin E.

The Antibody Society presents:



Antibody Validation Webinar Series

Visit our Learning Center to register for upcoming and On Demand webinars!

The Antibody Society has invited leaders in antibody research from industry and academia to reflect on antibody validation. They paint a uniformly alarming picture of inadequacies at many levels – which encourages users to be highly aware of the consequences of inadequate tool antibody validation, which threaten their biological endeavors.

Series moderator: Dr. Simon Goodman, Science & Technology Program Manager, The Antibody Society

Next Webinar Broadcast:
Webinar #8: Protein Arrays and Mass Spectrometry

February 5, 2020, 9am Eastern Standard Time / 3pm Central European Time, 30 min. webinar + 15 min. chat

Dr. Fridtjof Lund-Johansen, Oslo University Hospital, and Dr. Mike Taussig, Cambridge Protein Arrays, look at array and immunoprecipitation-mass spectrometry technologies, which offer a broader and deeper image of antibody specificity and selectivity for validation, than classical validation technologies.

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From: The Antibody Society <membership@antibodysociety.org>
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Antibody News You Should Know

February 1 - 15, 2020

Antibody-based therapeutics are advancing in clinical development at a rapid rate and being approved in record numbers. Recent news about antibody-related events are summarized below. Follow the links for more details.

Curious about antibody therapeutics that entered clinical study recently?
Society members can now access updated data for antibodies evaluated in first-in-human studies that started in 2018 or 2019.
Log in and explore the data in the Members Only area!

Phase 2 study started

On February 6, 2020 Aduro Biotech, Inc. announced that the company earned a milestone payment under its worldwide licensing agreement with Merck for the **initiation of a Phase 2 clinical trial of MK-5890** in non-small cell lung cancer (NSCLC). The study (NCT04165096) will assess the efficacy and safety of pembrolizumab in combination with MK-5890 in patients with advanced squamous or non-squamous NSCLC who have been previously treated with anti-PD-L1 therapy.

- MK-5890 is a humanized agonist monoclonal antibody that binds to CD27 to provide a costimulatory signal that enhances T cell-mediated responses.

Marketing application updates

On February 3, 2020 GlaxoSmithKline plc announced that the European Medicines Agency (EMA) validated the **marketing authorisation application (MAA) for belantamab mafodotin** (GSK2857916) for the treatment of patients with relapsed or refractory multiple myeloma whose prior therapy included an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody. Belantamab mafodotin was accepted for accelerated assessment by the EMA's Committee for Human Medicinal Products. The application included data from the pivotal DREAMM-2 study (NCT03525678), which were recently published in The Lancet Oncology.

- Belantamab mafodotin is composed of an afucosylated, humanized IgG1 antibody targeting B-cell maturation antigen conjugated to monomethyl auristatin F.

On February 5, 2020 GlaxoSmithKline plc released 2019 full year results indicating that a **regulatory submission had been filed in US for dostarlimab** for the 2nd line treatment of recurrent endometrial cancer. If the application receives a Priority Review designation, then an action by FDA would be expected by the end of June 2020.

- Dostarlimab is a humanized IgG4 antibody targeting PD1.

Other news

On February 3, 2020 Cerecor Inc. announced it completed the previously announced **acquisition of Aevi Genomic Medicine**. Cerecor's clinical pipeline now include CERC-002 (formerly AEVI-002) for Crohn's disease and CERC-007 (formerly AEVI-007 or MEDI-2338) for auto-inflammatory diseases.

- CERC-002 is a human IgG4 antibody targeting LIGHT.
- CERC-007 is a human IgG1 antibody targeting IL-18.

On February 5, 2020 Xencor, Inc. announced it has granted an exclusive **worldwide license to develop and commercialize XmAb7195 to Aimmune Therapeutics**, Inc. XmAb7195 (renamed AIMab7195) was originally developed by Xencor for the treatment of allergic asthma. Aimmune initially plans to develop AIMab7195 as an adjunctive treatment with

select Characterized Oral Desensitized ImmunoTherapy (CODIT™) programs to explore treatment outcomes in patients with food allergies.

- AIMab7195 is a humanized, Fc-engineered anti-IgE antibody.

On February 5, 2020 Alector, Inc. announced that the FDA granted **Fast Track designation to AL101** for the treatment of patients with progranulin gene mutations causative of frontotemporal dementia. AL101, which is designed to restore progranulin levels in the brain, is currently being evaluated in a Phase 1 study (NCT04111666) in healthy volunteers. FDA granted AL101 orphan drug designation for the treatment of frontotemporal dementia in July 2019.

- **AL101is a human antibody targeting SORT1**, designed to increase PGRN levels in the brain of patients to counteract the damage sustained due to low PGRN levels in neurodegenerative disorders.

On February 11, 2020 PhaseBio Pharmaceuticals, Inc. announced that **PB2452 has been granted PRIority MEdicines (PRIME) designation by EMA** for reversal of the antiplatelet effects of ticagrelor in patients with uncontrolled major or life-threatening bleeding or requiring urgent surgery or an invasive procedure. The company plans to conduct a non-randomized, open-label Phase 3 trial of major bleeding and urgent surgical populations to support an MAA for PB2452.

- PB2452 is a human monoclonal antigen-binding fragment that binds to ticagrelor and its active metabolite AR-C124910XX, and is intended to reverse the antiplatelet effects of ticagrelor.

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Series moderator: Dr. Simon Goodman, Science & Technology Program Manager, The Antibody Society

Don't miss the last Webinar Broadcast of this series:
Webinar #10: Specific Detection Reagents: What's the Future?

February 19, 2020, 9am Eastern Standard Time / 3pm Central European Time, 45 min. webinar + 15 min. chat

Speaker: Prof. Andreas Plückthun

Future recombinant binding tools may avoid antibodies, and use diversified libraries based on small and versatile protein scaffolds, for example the DARPins (Designed Ankyrin Repeat Proteins). DARPins are single-chain, monodisperse, and non-immunogenic, and can be made rapidly and cheaply in bacteria in many formats. They can also be expressed in and on cells as non-aggregating fusion proteins with tunable valencies, which opens a wide range of previously- inaccessible approaches in cell biology and biochemistry.

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Our mailing address is:
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From: The Antibody Society <membership@antibodysociety.org>
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Antibody News You Should Know

February 15 - March 1, 2020

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Have you missed some "Antibody News You Should Know"?
Archived news from 2019 can now be found in the
Web Resources section of the Society's website.

New to the clinic

A **Phase 1 study (NCT04278144) of Bolt Therapeutics' BDC-1001** as a single agent and in combination with pembrolizumab in patients with advanced and HER2-expressing solid tumors started on February 24, 2020. Estimated enrollment is 390 participants and the primary completion date is January 31, 2023.

- BDC-1001 is an immune stimulating antibody conjugate consisting of an

anti-HER2 monoclonal antibody (mAb) conjugated to a TLR 7/8 dual agonist.

On February 27, 2020 iTeos Therapeutics Inc. announced that it has enrolled the first patient in a **Phase 1/2 study of EOS884448** (EOS-448). This open-label, dose-escalation study will assess the safety, pharmacokinetic, pharmacodynamic and preliminary clinical activity of EOS-448 in participants with advanced cancers.

- EOS884448 is an human IgG1 mAb targeting the TIGIT receptor, which interacts with CD155 expressed on antigen-presenting cells or tumor cells to down-regulate T cell and natural killer cell functions.

A Phase 1, multicenter, open-label, **first-in-human study (NCT04276415) of Daiichi Sankyo's DS-6157a** in patients with advanced gastrointestinal stromal tumor is due to start in March 2020. In the initial dose escalation phase of the study, patients will receive an intravenous infusion of DS-6157a at doses in the 1.6 mg/kg to 8 mg/kg range. This study was not yet recruiting patients when first posted on February 19, 2020.

- DS-6157a is an antibody-drug conjugate composed of an antibody targeting GPR20, a protease-cleavable GGFG linker, and the DXd topoisomerase 1 inhibitor.

Phase 3 study to start

A **Phase 3 study of PhaseBio Pharmaceuticals' PB2452** in ticagrelor-treated patients with uncontrolled major or life-threatening bleeding or requiring urgent surgery or invasive procedure is due to start in March 2020. Estimated enrollment is 300 participants and the primary completion date is December 31, 2023. This study was not yet recruiting patients when first posted on February 27, 2020.

- PB2452 is a neutralizing antibody antigen-binding fragment that binds to ticagrelor and its active metabolite AR-C124910XX, and is intended to reverse the antiplatelet effects of ticagrelor.

BLA to be submitted soon

On February 26, 2020 Y-mAbs Therapeutics, Inc. announced that it completed a positive Type B Pre-Biologics License Application meeting with the U.S. Food and Drug Administration (FDA) regarding a potential pathway for FDA approval of omburtamab for the treatment of patients with CNS/leptomeningeal

metastases from neuroblastoma. The company reached alignment with the FDA on an Accelerated Approval Pathway for omburtamab along with a rolling BLA submission. Y-mAbs Therapeutics expects to complete the **rolling BLA for omburtamab** within approximately 10 weeks, and is planning for submission of a Marketing Authorization Application in Europe in Q4 2020.

- Omburtamab is a radiolabeled murine mAb targeting B7-H3 (CD276), which is expressed by most human glial tumors and not normal neurons or glia.

Recent marketing approvals

On February 17, 2020 **Novartis announced the European Commission approved Beovu®** (brolucizumab) injection for the treatment of wet age-related macular degeneration (AMD). Beovu® (brolucizumab-dbll) was approved by FDA in October 2019, for the treatment of neovascular AMD, and it received Swissmedic approval in Switzerland and Australian TGA approval in January 2020, both for the treatment of wet AMD.

- Brolucizumab is a humanized antibody single-chain variable fragment that binds to the 3 major isoforms of human vascular endothelial growth factor (VEGF), thereby interfering with their interaction with receptors VEGFR-1 and VEGFR-2 and suppressing endothelial cell proliferation, neovascularization and vascular permeability.

On February 21, 2020 **FDA approved Vyepti™ (eptinezumab-jjmr)** for the preventive treatment of migraine in adults. The recommended dosage is 100 mg as an intravenous infusion over approximately 30 minutes every 3 months; some patients may benefit from a dosage of 300 mg. Lundbeck expects to submit eptinezumab for approval to regulatory authorities in the European Union during 2020, followed by submissions for approval in other regions. Development of eptinezumab was initiated by Alder BioPharmaceuticals, Inc., which was acquired by H. Lundbeck A/S in October 2019. Lundbeck has indicated that Vyepti will be available in April 2020.

- Eptinezumab-jjmr is a humanized immunoglobulin G1 monoclonal antibody specific for calcitonin gene-related peptide ligand. It is produced in Pichia pastoris yeast cells

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In other news

On February 13, 2020 **Light Chain Bioscience, announced that it achieved**

a milestone and received a payment under its research and collaboration agreement with Takeda Pharmaceutical Company Limited, which aims at developing bispecific antibodies with Factor VIII mimetic activity for the treatment of hemophilia A patients. Light Chain Bioscience, a brand of Novimmune SA, achieved the successful completion of the discovery phase and designation by Takeda of undisclosed bispecific antibodies as clinical development candidates with approval to advance to IND-enabling studies.

- Light Chain Bioscience focuses on the selective targeting of the checkpoint CD47, as well as T cell redirecting strategies

On February 18, 2020 **ALX Oncology announced that the FDA granted two Fast Track designations for its lead candidate, ALX148,** for the first-line treatment of patients with head and neck squamous cell carcinoma (HNSCC), and for the second-line treatment of patients with HER2-positive gastric or gastroesophageal junction (gastric/GEJ) carcinoma. Data supporting these Fast Track designations were based on an open-label, multicenter Phase 1 clinical trial of ALX148 in combination with pembrolizumab or trastuzumab.

- ALX148 is a fusion protein comprising an engineered high affinity CD47 binding domain of SIRPα linked to an inactive Fc region of human immunoglobulin.

Planning on attending a meeting soon?

Society members receive 10-20% discounts on registration fees for these upcoming meetings:

March 2-5 World ADC London **UK.**
Members receive a **10% discount** when using code TABS10

March 9-12 Cell Line Development & Engineering **US. Santa Clara, CA**
Members receive a 15**% discount** when using code Antibody15.

Mar 30 – Apr 1 Cell Engager Summit**. Boston, MA.**
Members receive a **10% discount** when using code TABS10

May 4-8 PEGS Boston
Members receive a **20% discount** when using code TAS20.

June 9-11 Antibody Engineering & Therapeutics Europe**. Amsterdam**
Members receive a **15% discount** when using code Antibody15.

June 22-23 [8th Antibody Industrial Symposium AIS2020](). **Montpellier, France**

Members receive a **20% discount** when using code AbS20.

June 23-25 [World ADC Asia](). **Tokyo, Japan.**

Members receive a **10% discount** when using code TABS10.

View All Upcoming Meetings

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Antibody News You Should Know

March 1 - 15, 2020

The Antibody Society is an authoritative source of information about antibody therapeutics development. We are pleased to provide semi-monthly summaries of recent news to our members. Follow the links below for more details.

Have you missed previous "Antibody News You Should Know"?
Archived news from 2019 can now be found in the
Web Resources section of the Society's website.

New to the clinic

On March 3, 2020 Shanghai Henlius Biotech, Inc. announced that the first patient was dosed in Taiwan in a Phase 1 study (HLX55-001; NCT04169178) of HLX55 for the treatment of advanced solid tumors refractory to standard therapy. This study is an open-label and dose escalation study including dose finding stage and expansion stage. In the dosing finding stage, the study will precede in two phases: 1) a modified accelerated titration design 2A phase; and 2) a traditional 3+3 dose escalation phase aimed at exploring the safety

and maximum tolerated dose of HLX55. Four dose levels are designed for HLX55 in this stage: 2.5, 5, 15, and 25 mg/kg/3 weeks. The 5 mg/kg/3 weeks will serve as the starting dose.

- HLX55 is an innovative humanized monoclonal antibody that binds the human c-MET Sema/PSI domain. The antibody inhibits c-MET activation by blocking the HGF ligand binding and promotes the degradation of c-MET.

A Phase 1, open-label, dose-escalation, and dose-expansion study (NCT04291079) to investigate the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of **SRK-181 alone and in combination with anti-PD-(L)1 antibody therapy in patients with locally advanced or metastatic solid tumors** is now recruiting patients, according to a March 10, 2020 update on clinicaltrials.gov. The study, sponsored by Scholar Rock, Inc., will determine the maximum tolerated dose or maximum administered dose of SRK-181 as a single agent or in combination with an anti-PD-(L)1 antibody and will determine the recommended Phase 2 dose.

- SRK-181 is a human antibody designed to bind to, and prevent the activation of, latent TGFβ1 with high affinity and high selectivity, as evidenced by minimal or no binding to latent TGFβ2 and latent TGFβ3 isoforms.

An open-label, multicenter, randomized, dose-escalation and extension, **Phase IA/IB study to evaluate safety and anti-tumor activity of RO7284755 alone or in combination with atezolizumab in participants with advanced and/or metastatic solid tumors** is due to start soon. This study will assess the effects of RO7284755 as a single agent and in combination with atezolizumab in adult participants with solid tumors considered responsive to checkpoint inhibition blockade. The maximum duration in the study for each participant will be up to 28 months. First posted on March 11, 2020, this study is sponsored by Hoffmann-La Roche and is not yet recruiting patients.

- RO7284755 is a PD-1 targeted IL-2 variant immunocytokine.

A first-in-human, Phase 1, open-label, multiple-ascending dose study (NCT04306224) to investigate the safety, tolerability, pharmacokinetics, pharmacodynamics, and clinical activity of **IMC-002 in subjects with metastatic or locally advanced solid tumors and relapsed or refractory lymphomas** is due to start soon. In Part 1 of the study, dose escalation will follow the traditional 3+3 design. Cohorts of 3 subjects will be given escalating doses of IMC-002 once every 2 weeks as an IV infusion over 60 minutes. In Part 2, the study may be amended to include expansion cohorts in selected

tumor types to further evaluate extended safety of IMC-002 at recommended Phase 2 dose in that tumor type. First posted on March 12, 2020, this study is sponsored by ImmuneOncia Therapeutics Inc., and is not yet recruiting patients.

- IMC-002 is a human IgG monoclonal antibody that binds human CD47 with an optimal affinity that maximizes efficacy (tumor phagocytosis) without causing hemagglutination.

Biologics license application news

On March 2, 2020 Pfizer Inc. and Eli Lilly and Company announced that the U.S. **Food and Drug Administration (FDA) accepted for review a Biologics License Application (BLA) for tanezumab** 2.5 mg administered subcutaneously (SC), which is being evaluated for patients with chronic pain due to moderate-to-severe osteoarthritis who have experienced inadequate pain relief with other analgesics. The BLA includes data from 39 Phase 1-3 clinical studies evaluating the safety and efficacy of tanezumab among more than 18,000 patients, including three Phase 3 studies evaluating SC administration of tanezumab in patients with moderate-to-severe osteoarthritis.

- Tanezumab is a humanized IgG2 kappa monoclonal antibody that targets and inhibits nerve growth factor. A330S, P331S mutations decrease the effector functions of the antibody.

On March 2, 2020 MorphoSys AG announced that the **FDA accepted MorphoSys' BLA and granted priority review for tafasitamab**, which is under review in combination with lenalidomide for the treatment of relapsed or refractory diffuse large B cell lymphoma (r/r DLBCL). The BLA submission is based on the primary analysis data from the L-MIND trial of tafasitamab in combination with lenalidomide in patients with r/r DLBCL and the retrospective observational matched control cohort Re-MIND evaluating efficacy outcomes of r/r DLBCL patients who received lenalidomide monotherapy. FDA’s goal date for a first action on the BLA is August 30, 2020.

- Tafasitamab is an humanized Fc-engineered monoclonal antibody directed against CD19.

Recent marketing approvals

On March 2, 2020 **FDA approved Sarclisa (isatuximab-irfc), in combination with pomalidomide and dexamethasone, for the treatment of adult**

patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor. FDA granted isatuximab Orphan Drug designation for multiple myeloma. The approval was based on the results of the Phase 3 ICARIA-MM study (NCT02990338) demonstrating a statistically significant improvement in progression-free survival (PFS). The European Medicines Agency is currently evaluating a marketing authorization application for isatuximab for the treatment of relapsed/refractory multiple myeloma.

- Developed by Sanofi, isatuximab (SAR650984) is a chimeric IgG1 antibody directed against CD38 expressed on malignant plasma cells. The antibody acts through a combination of mechanisms, which may depend on the expression level of the target.

In other news

On March 10, 2020 The Janssen Pharmaceutical Companies of Johnson & Johnson announced that the **FDA granted Breakthrough Therapy Designation for JNJ-61186372 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. The Breakthrough Therapy Designation is supported by data from a Phase 1, first-in-human, open-label, multicenter study (NCT02609776).

- JNJ-61186372 (amivantamab) is a bispecific human IgG1 antibody that binds EGFR and mesenchymal epithelial transition factor (MET). The antibody targets activating and resistant EGFR and MET mutations and amplifications.

On March 12, 2020 Agenus Inc. announced that the **FDA granted Fast Track designation to balstilimab in combination with zalifrelimab for the treatment of patients with relapsed or refractory metastatic cervical cancer**. This designation was based on comprehensive data that support the potential for balstilimab and zalifrelimab to address a significant unmet medical need. Agenus expects to file 2 BLAs this year for accelerated approval of the combination of balstilimab and zalifrelimab and balstilimab monotherapy in metastatic cervical cancer.

- Balstilimab (AGEN2034) is a human IgG4 anti-PD-1 antagonist antibody, and zalifrelimab is a human IgG1 antibody targeting CTLA-4.

From: The Antibody Society <membership@antibodysociety.org>
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Subject: Antibody News You Should Know: March 15 - April 1, 2020

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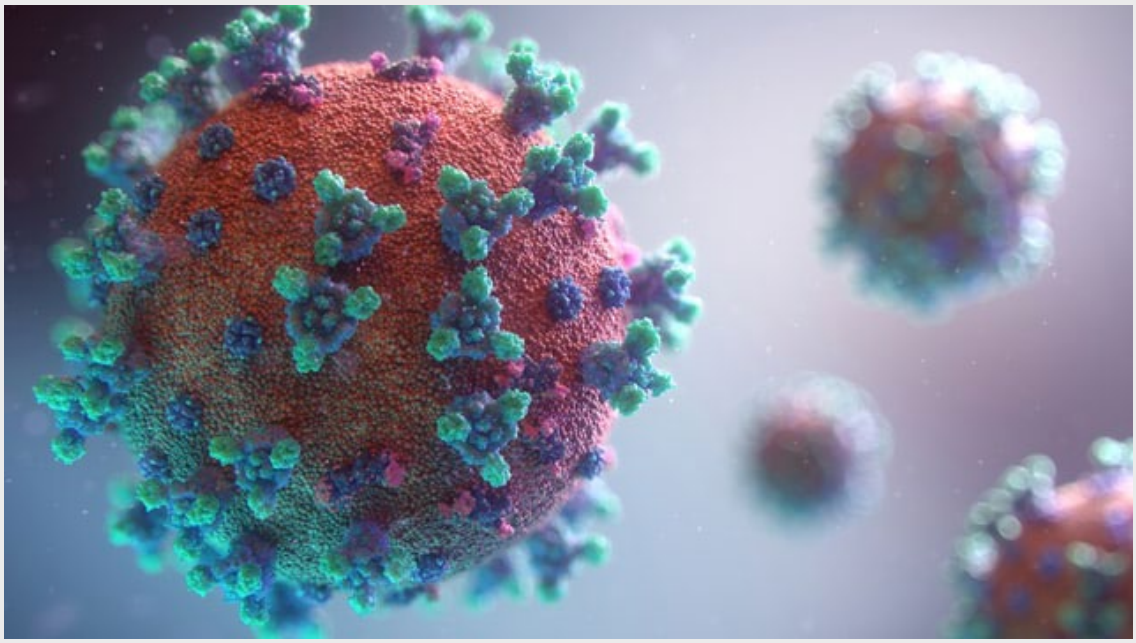

Antibody News You Should Know

March 15 - April 1, 2020

Special Issue:

COVID-19 Interventions

Biopharmaceutical companies, government agencies, academic institutions and non-profits located world-wide have mobilized in an unprecedented effort to develop interventions that are effective against SARS-CoV-2, the virus that causes COVID-19.

The Antibody Society's series **"Coronavirus in the crosshairs"** examines the ongoing discovery and development of COVID-19 interventions for broad use, including small molecule and biologic drugs, and vaccines.

- **Part 1** examines re-purposed small molecule and biologic drugs;
- **Part 2** reviews new vaccines in development;
- **Part 3** focuses on COVID-19 convalescent plasma treatments in development; and
- **Part 4** provides additional details about re-purposed biologics, such as monoclonal antibodies that are marketed or in clinical studies for other indications, that might ameliorate COVID-19 symptoms and that are already in clinicals studies of COVID-19 patients. We also discuss anti-SARS-CoV-2 antibodies that are in preclinical development and may enter clinical study by the end of 2020.

The specific content of the posts is prioritized based on when the interventions might be available to either patients or healthy people, including health care workers. Re-purposed small molecule and biologic drugs are likely to be available first, followed by new vaccines and drugs.

The Antibody Society will alert the scientific community to new information about COVID-19 interventions via our website, social media, and email to our members.

Update on antibody-based COVID-19 interventions in development

Numerous organizations and groups have announced plans or progress in developing antibody-based interventions for COVID-19. The race will go to the swift, in this case organizations that are:

- Already experienced in anti-infective antibody discovery;
- Adept at antibody design, engineering and selection;

- Able to manufacture antibodies; and
- Experienced in regulatory affairs.

If any of these elements are missing, then the organization will need to quickly contract the work or engage a collaborator or partner with the missing expertise.

It must be noted, however, that a single product is unlikely to meet the currently very substantial medical need, and not all product candidates will be successful in clinical studies. Therefore, ***many initiatives aimed at developing investigational antibodies are needed.***

The development of anti-SARS-CoV-2 antibody therapeutics involves the following major steps:

- Initiation of the discovery process using, e.g., transgenic mouse, display technology or human B cell from COVID-19 patient;
- Identification and characterization of suitable antibodies via in vitro methods;
- Non-clinical assessment via in vivo methods;
- Manufacturing of material suitable for administration to humans;
- Demonstration of safety and efficacy in humans.

Due to the severity of the pandemic, the pace of the process, which typically is quite slow, has been substantially accelerated.

At least 8 organizations or groups have announced that their antibody-based interventions for COVID-19 are on track to enter clinical study soon. For example:

- **Shanghai Junshi Biosciences Ltd**. and the Institute of Microbiology of the Chinese Academy of Sciences are developing neutralizing antibodies derived from patients who recovered from COVID-19 as a potential treatment for COVID-19. The program will progress to clinical trials soon. According to a March 24, 2020 announcement, they have obtained neutralizing antibodies that can effectively block viral invasion in laboratory assays, conducted animal experiments, and are now verifying the preclinical toxicology and in vivo activity of the antibodies. An investigational new drug application, needed to initiate clinical studies, is in preparation.
- **Mabpharm Limited** has generated a mAb-based fusion protein (CMAB020, STI-4920, ACE-MAB) that binds to the spike protein of the SARS-CoV-2 virus. Designed as a bispecific molecule, ACE-MAB has two functional arms: 1) a human antibody that targets the spike protein of

SARS-CoV-2 with high affinity and 2) a truncated ACE2 protein that binds to a different epitope of the spike protein. ACE-MAB is in the cGMP cell line development stage by Mabpharm Limited, and could be ready for large-scale production for human clinical trials and commercialization upon receipt of requisite regulatory approvals. Mabpharma and Sorrento Therapeutics, Inc. have partnered in the development of ACE-MAB.

- **Vir Biotechnology, Inc.**, working with partners Xencor, Biogen and WuXi, has identified multiple human monoclonal antibody candidates that neutralize SARS-CoV-2. Two candidates will progress into human testing as soon as possible, with Phase 1/2 clinical testing planned for summer 2020.
- **Regeneron Pharmaceuticals** has isolated virus-neutralizing, human antibodies from transgenic VelocImmune® mice, and antibodies from COVID-19 patients. From this large pool of candidates, Regeneron will select the top two antibodies for a 'cocktail' treatment based on potency and binding ability to the SARS-CoV-2 spike protein, as well as other desirable qualities. Regeneron aims to have an anti-SARS-CoV-2 antibody treatment ready for human testing by early summer.
- **Sorrento Therapeutics** announced that STI-4398 is in the cGMP cell line development stage and could be ready for large-scale production in Sorrento's cGMP facilities in San Diego for human clinical trials and commercialization upon receipt of requisite regulatory approvals. STI-4398 is a proprietary ACE2 (angiotensin-converting enzyme 2)-Fc fusion protein (COVIDTRAP). The STI-4398 protein binds to the S1 domain of the spike protein, which is expected to block the spike protein of the SARS-CoV-2 virus to bind the ACE2 receptors present on the target respiratory epithelial cells.
- **Vanderbilt University Medical Center**, in collaboration with academic, governmental and corporate partners has already discovered SARS-CoV-2 antibodies. The collaborators aim to have antibodies for human clinical trials by summer 2020.
- **Coronavirus Immunotherapy Consortium** plans to use Carterra's proprietary LSA™ platform, which can screen hundreds of antibodies in just a few days, to move therapeutic candidates to the clinic as early as this summer.
- **Celltrion** has identified a library of antibodies sourced from the blood of recovered COVID-19 patients in Korea. These antibodies are undergoing further screening to identify those that are most effective in neutralizing SARS-CoV-2. Selected candidates will form the basis of anti-viral treatment to be tested in preclinical and clinical trials in the third quarter of

2020.

Lists of COVID-19 interventions in development

The Antibody Society will continue to collect data and report on progress with the development of COVID-19 interventions. Other organizations are also providing data for COVID-19 interventions:

- **BioWorld**: Biopharma products in development for COVID-19
- **Regulatory Affairs Professionals Society**: COVID-19 Tracker
- **Milken Institute**: COVID-19 Treatment and Vaccine Tracker
- **World Health Organization**: Landscape of COVID-19 candidate vaccines
- **PhRMA**

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