#### Antibodies to watch in a pandemic

Speakers:

Dr. Janice M. Reichert, Executive Director, The Antibody Society Dr. Thomas Schirrmann, CEO, Yumab

June 30, 2020

ANTI BODY SOCI

#### Agenda

- Update on Antibodies to watch in 2020
  - Antibody therapeutics approved in 2020 as of June 15
  - Antibody therapeutics that may be approved by the end of 2020.
- Overview of antibody-based COVID-19 interventions in development
  - Repurposed antibody-based therapeutics that treat symptoms
  - Newly developed anti-SARS-CoV-2 antibodies
- Yumab's approach to anti-SARS-CoV-2 antibody therapeutics
  - Accelerated development via academic / industrial consortium
- Q&A

#### Annual first approvals in either the US or EU



\*Estimate based on the number actually approved and those in review as of June 1, with assumption of approval on the first cycle. Tables of approved mAbs and antibodies in review available at <u>https://www.antibodysociety.org/resources/approved-antibodies/</u>

#### First approvals US or EU in 2020

- Teprotumumab (Tepezza): anti-IGF-1R mAb for thyroid eye disease
  - FDA approved on January 21
- Eptinezumab (Vyepti): anti-CGRP IgG1 for migraine prevention
  - FDA approved on February 21
- Isatuximab (Sarclisa): anti-CD38 IgG1 for multiple myeloma
  - FDA approved on March 2; approved in EU on June 2
- Sacituzumab govitecan (Trodelvy): anti-TROP-2 ADC for triple-neg. breast cancer
  - FDA approved on April 22
- Inebilizumab-cdon (Uplizna): anti-CD19 IgG1 for the treatment of neuromyelitis optica spectrum disorder
  - FDA approved on June 11
- See Antibodies to watch in 2020 for more information: <u>https://www.tandfonline.com/doi/full/10.1080/19420862.2019.1703531</u>

• Complete list of US- and EU-approved mAbs (1986 to present) and antibodies in review available at: <a href="https://www.antibodysociety.org/resources/approved-antibodies/">https://www.antibodysociety.org/resources/approved-antibodies/</a>

### Potential approvals in 2020: 16 in US or EU regulatory review

#### US or EU review: PDUFA dates July-Aug

- Belantamab mafodotin: anti-BCMA IgG1 ADC for multiple myeloma
  - US and EU review; late July PDUFA date
  - Breakthrough Therapy (US) and PRIME (EU) designations
- Satralizumab: anti-IL-6R for NMOSD
  - US and EU review; accelerated assessment in EU; late August PDUFA date
- Tafasitamab (MOR208): anti-CD19 IgG1 for diffuse large BCL
  - US review, Breakthrough Therapy, Fast Track, Orphan Drug designations in US; August 30 PDUFA date

#### US or EU review: PDUFA dates Sep-Dec

- REGN-EB3: mixture of 3 IgG1 mAbs for Ebola virus infection
  - US review, Breakthrough Therapy designation; October 25 PDUFA date
- Sutimlimab: anti-C1s IgG4 for cold agglutinin disease
  - US review, Breakthrough Therapy designation; November 13 PDUFA date
- Naxitamab: anti-GD2 lgG1 for neuroblastoma
  - US review; Rare Pediatric Disease, Breakthrough Therapy, Orphan designations; November 30 PDUFA date
- Margetuximab: anti-HER2 IgG1 mAb for breast cancer
  - US review, Fast Track designation; December PDUFA date
- Tanezumab: anti-NGF lgG2 for osteoarthritis pain
  - US and EU review, Fast Track designation; December PDUFA date



#### US review (non-cancer): PDUFA date unknown

- Leronlimab: anti-CCR5 IgG4 for HIV infection
  - US review; Fast Track designation, rolling BLA
- Narsoplimab: anti-mannan-binding lectin-associated serine protease-2 (MASP-2) IgG4 for hematopoietic stem cell transplant-associated thrombotic microangiopathy
  - US review; Breakthrough Therapy designation, rolling BLA
- Aducanumab: anti-amyloid  $\beta$  IgG1 for early Alzheimer's disease
  - US review; Fast Track designation, rolling BLA; PRIME designation
- Evinacumab: anti-angiopoietin-like protein 3 IgG4 for hypercholesterolemia
  - US review; Breakthrough Therapy designation
- Teplizumab (PRV-031): anti-CD3 IgG1 for type 1 diabetes
  - US review; Breakthrough Therapy designation, PRIME designation

#### US review (cancer): PDUFA date unknown

- Oportuzumab monatox (Vicineum<sup>®</sup>): anti-EpCAM scFv immunotoxin for bladder cancer
  - US review; Fast Track designation; FDA aligned with use of Accelerated Approval pathway with rolling review
- Dostarlimab (TSR-042): anti-PD-1 lgG4 for recurrent MSI-H tumors
  - US and EU review

- See Antibodies to watch in 2020 for more information: <a href="https://www.tandfonline.com/doi/full/10.1080/19420862.2019.1703531">https://www.tandfonline.com/doi/full/10.1080/19420862.2019.1703531</a>
- Complete list of US- and EU-approved mAbs (1986 to present) and antibodies in review available at: <u>https://www.antibodysociety.org/resources/approved-antibodies/</u>

#### EU review

- Tralokinumab: anti-IL-13 IgG4 for atopic dermatitis
  - EU review
  - Validation of marketing authorization application by the European Medicines Agency announced by LEO Pharma on June 11, 2020

- See Antibodies to watch in 2020 for more information: <u>https://www.tandfonline.com/doi/full/10.1080/19420862.2019.1703531</u>
- Complete list of US- and EU-approved mAbs (1986 to present) and antibodies in review available at: <u>https://www.antibodysociety.org/resources/approved-antibodies/</u>

#### Overview of antibody-based COVID-19 interventions





#### COVID-19 resources at antibodysociety.org

- "Coronavirus in the Crosshairs"
  - 9-part (so far) series examining the ongoing discovery and development of COVID-19 interventions for broad use, including small molecule and biologic drugs, and vaccines. Diagnostics are also discussed.
  - <a>www.antibodysociety.org/guide-to-coronavirus-in-the-crosshairs/</a>
- COVID-19 Biologics Tracker
  - Information for clinical studies of anti-SARS-CoV-2 antibodies
    - www.antibodysociety.org/covid-19-biologics-tracker/
  - Link to COVID-19 Antibody Therapeutics Tracker
    - <u>chineseantibody.org/covid-19-track/</u>

#### Antibody-based COVID-19 interventions

- The Antibody Society, in collaboration with the Chinese Antibody Society, is tracking ~130 antibody-based COVID-19 interventions sponsored by commercial firms
  - 45 (~35%) are 'repurposed' biologics intended as treatments for symptoms
  - 84 (~65%) are novel biologics that target SARS-CoV-2, typically the spike protein
- Data are collected from the public domain, and <u>therefore likely</u> represent only a portion of the ongoing efforts.
- Programs sponsored by solely academic/government organizations are not included here, but are included in the Tracker database.

# Repurposed antibody-based therapies as possible treatments for symptoms

#### Medical conditions associated with COVID-19

- Disease caused by coronavirus infection, which leads to:
  - Cytokine storm-induced acute respiratory distress syndrome
  - Moderate to severe COVID-19 pneumonia
  - Tissue damage resulting from hyper-inflammation, e.g., multisystem inflammatory syndrome in children
  - Abnormal clotting
- Numerous proteins involved in disease-associated pathways (e.g., pro-inflammatory cytokines) are targets for over 40 antibody-based therapeutics development.
  - Relevant targets include: IL-1, IL-6, IL-8, GM-CSF

## Frequent targets of antibodies for COVID-19 symptoms



Number of antibodies

ANTI BODY SOCI . ETY

#### Less frequent targets (1-2 antibodies\*)

✓ Ang-2, C2, CCR5, CD14, CD6, CXCL10, connective tissue growth factor, CSF1R/CD115;

✓ Danger-associated molecular patterns (DAMPS), Factor XIIa;

✓IFNγ, IL-1, IL-17A, IL-22R, IL-33R, IL-8;

✓ LIGHT, Neutrophilin 2, Nicotinamide phosphoribosyltransferase;

✓ NKG2A, Plasma kallikrein, P-selectin, TLR4

✓ Staph. aureus  $\alpha$  toxin, VEGF, Vimentin

\*For details about the antibodies, see <u>chineseantibody.org/covid-19-track/</u>

#### Most advanced phase of development\*



■ For COVID ■ For any disease

\*Includes pending clinical studies listed on clinicaltrials.gov. Phase 2 = Phase 1/2 + Phase 2; Phase 3 = Phase 2/3 + Phase 3

> ANTI BODY SOCI . ETY

#### Authorized as therapy for COVID-19

- Levilimab (trade name Ilsira) registered in Russia for treatment of patients with severe COVID-19.
  - Human mAb targeting membrane-bound and soluble forms of IL-6R
  - Developed by Biocad, levilimab was originally developed for treatment of rheumatoid arthritis.
  - Phase 3 study was initiated on April 24, 2020, and includes 204 participants who received a single subcutaneous administration of levilimab at a dose of 324 mg in combination with standard therapy.
  - According to Biocad, the results of a clinical trial of the drug demonstrate that <u>levilimab therapy can significantly reduce mortality</u> among patients with COVID-19.
  - Registered on June 5, 2020 through a fast-track mechanism according to Decree No. 441 of the Government of the Russian Federation, effective as of April 4, 2020.

#### Most advanced in clinical studies for COVID-19

- *Of the 16 in late-stage studies* for COVID-19, 6 are already approved for another indication
  - Anti-IL-6R Tocilizumab
    - First approved in Japan in 2005. <u>Currently marketed</u> for rheumatoid arthritis in adults, juvenile rheumatoid arthritis, treatment of chimeric antigen receptor T cell-induced *severe or life-threatening cytokine release syndrome* (CRS) in patients two years of age and older. <u>Tocilizumab is included in over 55 clinical studies of COVID-19 patients, 3 of which are Phase 3 studies sponsored by Genentech/Roche.</u>
    - 3 Phase 3 studies of patients with COVID-19 pneumonia sponsored by Genentech/Roche have primary completion dates of:
      - July 31, tocilizumab +remdesivir vs remdesiver only; recruiting 450 patients at 32 study sites
      - <u>Aug 5</u>, recruiting 379 patients at 32 study sites
      - <u>Aug 31</u>, 450 patients; study is active but not recruiting at 68 study sites

#### More mAbs targeting IL-6/R for COVID-19

- Anti-IL-6R Sarilumab
  - Approved for rheumatoid arthritis
  - 15 COVID-19 studies include sarilumab, 5 are Phase 3 studies
  - 2 of the Phase 3 studies are sponsored by Sanofi/Regeneron and have primary completion dates in:
    - July 2020, recruiting 400 hospitalized patients at 45 study sites
    - May 2021, recruiting 2500 hospitalized patients at 65 study sites
- Anti-IL-6 Siltuximab
  - Approved for multicentric Castleman's disease
  - 3 COVID-19 studies include siltuximab, 1 is a Phase 3 study
  - None are sponsored by a commercial firm

#### More in late-stage clinical studies for COVID-19

- Marketed mAbs
  - Anti-IFNγ Emapalumab
    - Approved for primary hemophagocytic lymphohistiocytosis
  - Anti-IL-1 $\beta$  Canakinumab
    - Approved for adult-onset Still's disease, juvenile rheumatoid arthritis, cryopyrin (CIAS1)associated periodic syndromes, tumor necrosis factor receptor-associated periodic syndrome, hyperimmunoglobulin D syndrome / mevalonate kinase deficiency, familial Mediterranean fever in combination with colchicine
  - Anti-C5 Ravulizumab (Phase 3 pending)
    - Approved for paroxysmal nocturnal hemoglobinuria
- And 1 is in FDA review for HIV infection
  - Anti-CCR5 Leronlimab

#### Next steps for repurposed biologics

- Possible FDA Emergency Use Authorization (EUAs)
  - FDA can <u>allow use of unapproved medical products or unapproved uses of approved medical products</u> to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by threat agents, such as SARS-CoV-2, when there are no adequate, approved, and available alternatives.
- Limitations to the scope and duration of the authorizations, as well as specific conditions, apply to EUAs
- FDA's allowance of an *emergency investigational new drug* application or compassionate use of a COVID-19 intervention is <u>not</u> equivalent to FDA issuing an EUA, and EUA issuance is <u>not</u> equivalent to FDA approval
- Sponsoring organizations may or may not pursue EUAs

#### Anti-SARS-CoV-2 antibodies

#### Characteristics of anti-SARS-CoV-2 biologics

✓ Of over 80 we are currently tracking:

- ✓~88% are traditional mAb-based therapeutics, incl. nanobodies
- ✓~12% are other composition of matter (e.g., DARPin, Fc fusion protein, nucleic acid) or recombinant or transgenic animal-derived polyclonals

 $\checkmark$  Of the mAbs with known derivations (~70% of total):

- ✓ 48% are derived from B cells of convalescent patients
- ✓ 27% are derived from in vitro methods (e.g., phage display)

 $\checkmark$  25% are derived from immunization of animals

✓ Some organizations are using 2 or all 3 of these methods.

#### Most advanced phase of development\*



\*Estimated from public disclosures as of June 1, 2020

Discovery phase = Screening and assessment of neutralization

Preclinical phase = Protection in animal model, cell line development, preparation for clinical study

ANTI BODY SOCI . ETY

#### Anti-SARS-CoV-2 antibodies in clinical study\*

Sponsors	Drug code	Status	Trial ID	Est. start	Est. primary completion
Junshi Biosciences / Eli Lilly and Company	JS016	Phase 1	NA, study sites in China	6/7/2020	NA
Tychan Pte. Ltd.	TY027	Phase 1	<u>NCT04429529</u>	6/9/2020	Oct. 2020
Regeneron	REGN-COV2 (REGN10933 + REGN10987)	Phase 1/2/3	NCT04425629 (Phase 1/2/3); NCT04426695 (Phase 1/2/3)	6/9/2020; 6/12/2020	11/21/2020; 3/13/2021
AbCellera / Eli Lilly and Company	LY-CoV555, LY3819253	Phase 2	NCT04411628 (Phase 1); NCT04427501 (Phase 2)	5/28/2020; 6/13/2020	8/23/2020; 9/15/2020

\*As of June 15, 2020

#### Antibodies to watch during June – Dec 2020\*

- "<u>Coronavirus in the Crosshairs, Part 9</u>" notes over 15 companies plan to progress anti-SARS-CoV-2 molecules into the clinic by the end of 2020, including:
  - Yumab/CORAT Therapeutics, with partners
  - Celltrion
  - Vir Biotechnology, Inc. / Humabs Biomed SA, with partners
  - Sorrento Therapeutics, with partners
  - AstraZeneca, with partners, e.g., Vanderbilt University Medical Center
  - Centivax/ Distributed Bio / SwiftScale Biologic
  - Virna Therapeutics / University of Toronto
  - Shanghai Junshi Biosciences Co., Ltd
  - Molecular Partners (DARPin molecule)

\*For details about these antibodies, see chineseantibody.org/covid-19-track/

ANTI BODY SOCI . ETY

#### Key messages

- Projections indicate that 2020 may be a record year for approvals of antibody therapeutics *if the regulatory agencies resources are not diverted to COVID-19-related work*
- FDA Emergency Use Authorizations are likely for at least some of the repurposed mAbs, with EUAs likely soonest for anti-cytokine mAbs, e.g., tocilizumab
- The extraordinary response by numerous organizations developing anti-SARS-CoV-2 antibodies may lead to EUAs for 15-20 antibodies, <u>if sponsoring organizations pursue this route</u>, with the first EUA possible as early as September 2020.





BIOCYTOGEN

biotechne

Boehringer Ingelheim









A Member of the Roche Group



#### Support also provided by...



'• Genmab

...ichnos...

**Y** ImmunoPrecise

> L XVA therapeutics

IONTAS



LIGHTCHAIN BIOSCIENCE









#### Support also provided by...















#### The next speaker is:

#### Dr. Thomas Schirrmann CEO, Yumab