Antibodies to Watch in 2021:
Anti-SARS-CoV-2 antibodies to the rescue

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Agenda

- Anti-SARS-CoV-2 antibody therapeutics
  - Late-stage clinical development
  - Emergency use authorizations
- US or EU approvals in 2020, and those expected in 2021
  - Granted as of December 1, 2020
  - Antibody therapeutics in regulatory review
- Potential marketing application submissions by the end of 2021

Anti-SARS-CoV-2 antibody therapeutics

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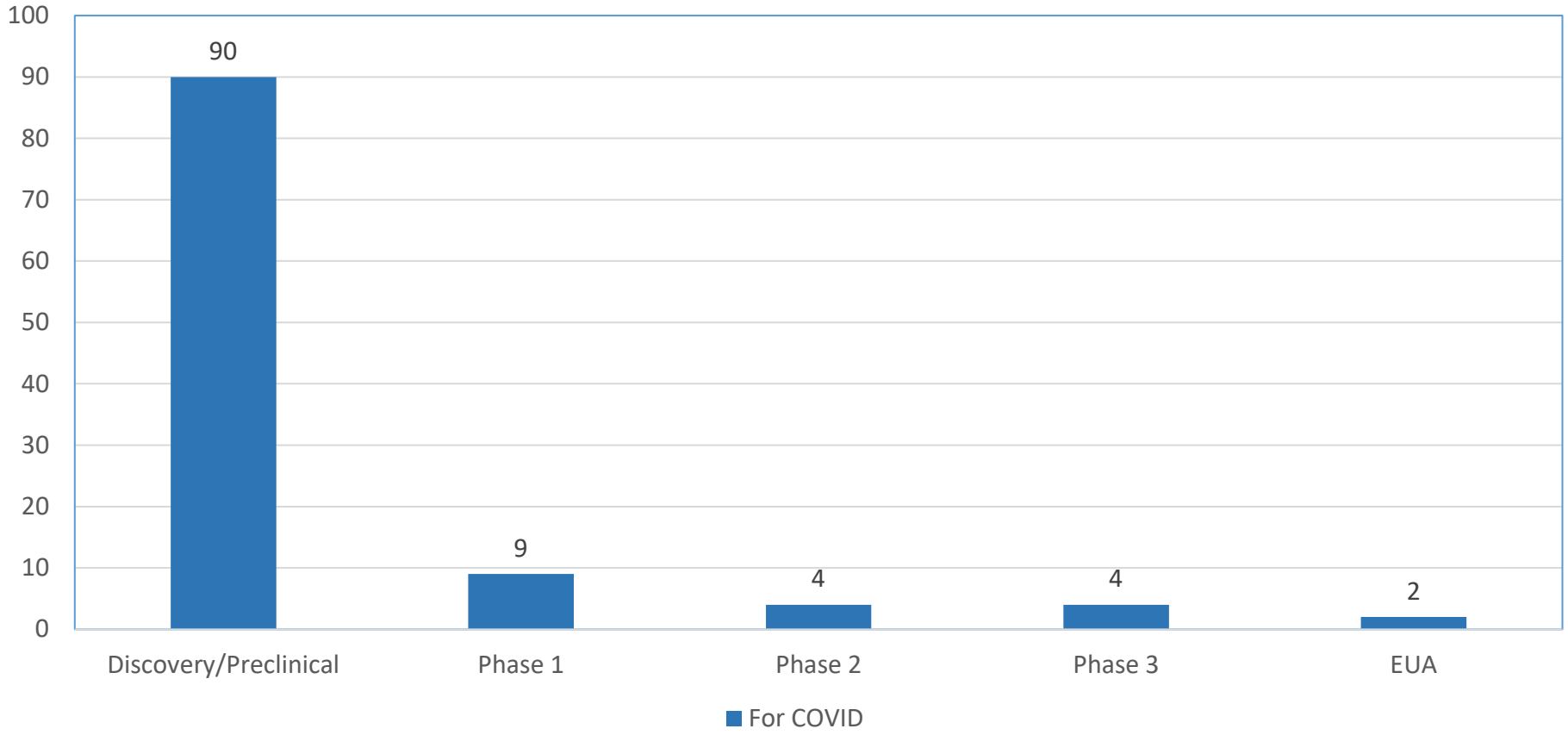
Characteristics of anti-SARS-CoV-2 biologics

- Of ~122 commercially sponsored molecules/programs we are currently tracking:
  - ~88% are 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)
- SARS-CoV-2 target is the Spike protein, according to the available information

mAbs: Most advanced phase of development*



*Based on public disclosures as of Nov 20, 2020. Phase 1/2 included with Phase 2; Phase 2/3 included in Phase 3. Totals includes pending studies. More information at: www.antibodysociety.org/covid-19-biologics-tracker/

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Anti-SARS-CoV-2 Antibodies to Watch in 2021

Sponsors	Drug codes	Status	Trial ID	Est. primary completion
Sinocelltech	SCTA01	Phase 2/3 pending	NCT04644185	May 2021
AstraZeneca	AZD7442	Phase 3 pending	NCT04625725; NCT04625972	Jul 2021; Jun 2021
Celltrion	CT-P59	Phase 2/3	NCT04602000	Dec 2020
Vir Biotechnol./ GSK	VIR-7831/ GSK4182136	Phase 2/3	NCT04545060	Jan 2021
AbCellera / Eli Lilly and Co.	LY-CoV555	EUA on 11/9/2020	NCT04497987(Phase 3); NCT04518410 (Activ-2) NCT04501978 (Activ-3);	Mar 2021; Nov 2020 Jul 2021;
Regeneron	REGN-COV2 (REGN10933 + REGN10987)	EUA on 11/20/2020	NCT04425629 (Phase1/2); NCT04426695 (Phase1/2); NCT04452318 (Phase 3)	Dec 2020; Jan 2021; Jun 2021

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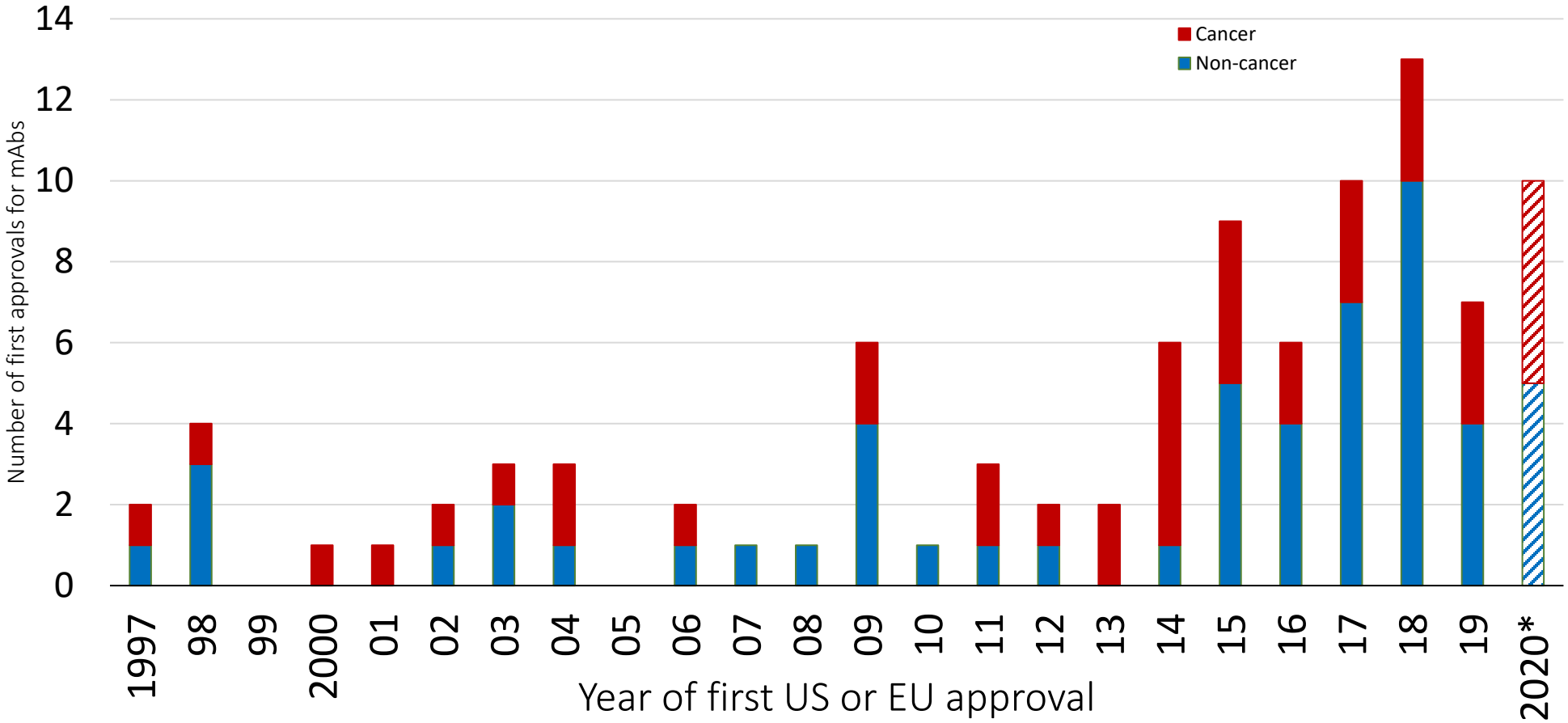
EUAs granted as of Nov 20, 2020

- Lilly's bamlanivimab (LY-CoV555) monotherapy in higher-risk patients who have been recently diagnosed with mild-to-moderate COVID-19.
  - Lilly will receive $375 million for 300,000 doses purchased by the US government. According to Lilly, up to 100,000 doses of 700 mg LY-CoV555 monotherapy may be available in October, and one million doses available in Q4 2020.
  - Estimated price per vial (0.7 g) is $1250. ($375 million/300,000 doses)
  - Lilly anticipates submission of an EUA request for combination therapy in November, and may have data to support a biologics license application submission for combination therapy as early as Q2 2021.
- Regeneron's casirivimab and imdevimab low dose (2.4 g) in adults with mild-to-moderate COVID-19 who are at high risk for poor outcomes.
  - Regeneron was granted a $450 million contract to manufacture and supply REGN-COV2 by the US government, which has committed to making the doses available to Americans for free. At the time of the EUA request, Regeneron had doses available for ~ 50,000 patients, and expects to have doses available for a total of 300,000 patients within several months.
  - Estimated price per vial (2.4 g) is $1500. ($450 million/300,000 doses)

US/EU approvals in 2020

Annual first approvals in either the US or EU



*10 antibody therapeutics approved as of Nov 30, 2020; 2 (Margetuximab, Tanezumab) may be approved by the end of 2020.
Tables of approved mAbs and antibodies in review available at https://www.antibodysociety.org/resources/approved-antibodies/

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 the 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

Complete list of US- and EU-approved mAbs (1986 to present) and antibodies in review available at:
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First approvals US or EU in 2020

- Tafasitamab (MOR208): anti-CD19 IgG1 for diffuse large BCL
  - FDA approved on July 31, 2020; EU review
  - Breakthrough Therapy, Fast Track, Orphan Drug designations in US
- Belantamab mafodotin: anti-BCMA IgG1 ADC for multiple myeloma
  - FDA approved on August 5, 2020; approved in EU on Aug 25
  - Breakthrough Therapy (US) and PRIME (EU) designations
- Satralizumab: anti-IL-6R for NMOSD
  - FDA approved on August 14, 2020
  - EU review; accelerated assessment in EU
- REGN-EB3: mixture of 3 IgG1 mAbs for Ebola virus infection
  - FDA approved on October 14, 2020
  - Breakthrough Therapy designation
- Naxitamab: anti-GD2 IgG1 for neuroblastoma
  - FDA approved on November 25, 2020
  - Rare Pediatric Disease, Breakthrough Therapy, Orphan designations

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Potential approvals in 2020/21: 16 in US or EU regulatory review

US or EU review: PDUFA dates in Dec 2020

- Margetuximab: anti-HER2 IgG1 mAb for breast cancer
  - US review, Fast Track designation
- Tanezumab: anti-NGF IgG2 for osteoarthritis pain
  - US and EU review, Fast Track designation

US review: PDUFA date unknown

- 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
- Dostarlimab (TSR-042): anti-PD-1 IgG4 for recurrent MSI-H tumors
  - US and EU review

2021 approvals: PDUFA estimates known

- Evinacumab: anti-angiopoietin-like protein 3 IgG4 for hypercholesterolemia
  - US review and EU review; Breakthrough Therapy designation
  - Feb 11, 2021 PDUFA date
- Aducanumab: anti-amyloid β IgG1 for early Alzheimer's disease
  - US review and EU review; Fast Track designation, rolling BLA; PRIME designation
  - March 7, 2021 PDUFA date
- Loncastuximab tesirine: anti-CD19 humanized IgG1 ADC for diffuse large BCL
  - US review; Orphan Drug designation
  - May 21, 2021 FDA action date
- Tralokinumab: anti-IL-13 IgG4 for atopic dermatitis
  - US and EU review
  - PDUFA date in Q2 2021
- Anifrolumab: anti-IFN α, β, ω R1 for systemic lupus erythematosus
  - US and EU review; Fast Track designation
  - PDUFA date September 30, 2021

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More possible 2021 approvals

- Teplizumab (PRV-031): anti-CD3 IgG1 for type 1 diabetes
  - US review; Breakthrough Therapy designation, PRIME designation
- Inolimomab: anti-CD25 murine mAb for acute graft-vs-host disease
  - US review
- Ansuvimab: anti-Ebola virus human IgG1 for Ebola infection
  - US review
- Bimekizumab: anti-IL-17A humanized IgG1 for psoriasis
  - US and EU review
- Sutimlimab: anti-C1s IgG4 for cold agglutinin disease
  - US review, Breakthrough Therapy designation

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More possible 2021 approvals

- Oportuzumab monatox (Vicineum®): anti-EpCAM scFv immunotoxin for bladder cancer
  - US review; Fast Track designation; FDA aligned with use of Accelerated Approval pathway with rolling review
- Balstilimab: anti-PD-1 human IgG4 for cervical cancer
  - US review; Fast Track designation

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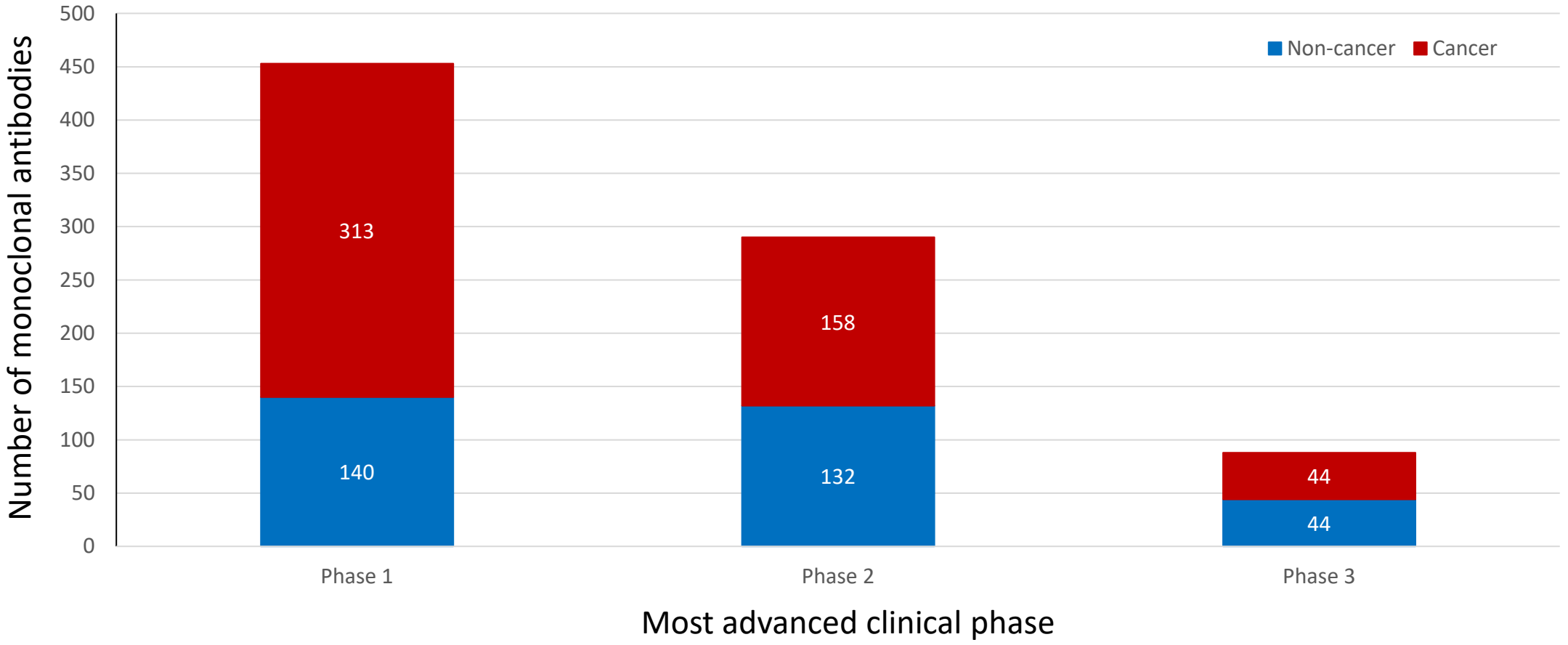
Marketing applications planned in 2020/21

- Many BLAs/MAAs may be submitted in the next 14 months
  - At least 6 for Non-cancer indications: 2021 submissions are planned for Leronlimab, Tezepelumab, Faricimab, Ligelizumab, Garetosmab, and Fasinumab.
  - At least 13 for Cancer indications: Submissions for I-131 omburtamab, trastuzumab duocarmazine, tisotumab vedotin, amivantamab and perhaps ublituximab are anticipated by the end of 2020, and applications may be submitted in 2021 for sabatolimab, zalifrelimab, cusatuzumab, AK104, cosibelimab, mirvetuximab soravtansine, apamistamab-I-131, and KN046
  - See "Antibodies to Watch in 2021" (antibodysociety.org/society-publications/) & published in *mAbs*

Antibody therapeutics clinical pipeline*



*Includes commercial development only; molecules in Phase 1/2 and 2/3 studies incorporated as Phase 2 and Phase 3, respectively.
Figure based on data available as of September 2020.

Key messages

- Pandemic is likely to continue well into 2021, thus the global need for effective therapeutics and vaccines will not abate
- The extraordinary response by numerous organizations developing anti-SARS-CoV-2 antibodies may lead to EUAs for 15-20 antibodies or other targeted proteins (*assuming safety and efficacy are demonstrated*)
- Projections indicate that 2020 and 2021 may be at or near record levels for approvals of antibody therapeutics, despite the demands placed on the regulatory agencies by COVID-19
- Finally, watch for “Antibodies to Watch in 2021” publication in *mAbs* in Dec 2020/Jan 2021

Acknowledgements

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Thank you!

Questions?
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