Antibodies to watch in 2020

PEGS Europe, Lisbon
November 20, 2019

Janice M. Reichert, Ph.D.
Executive Director, The Antibody Society

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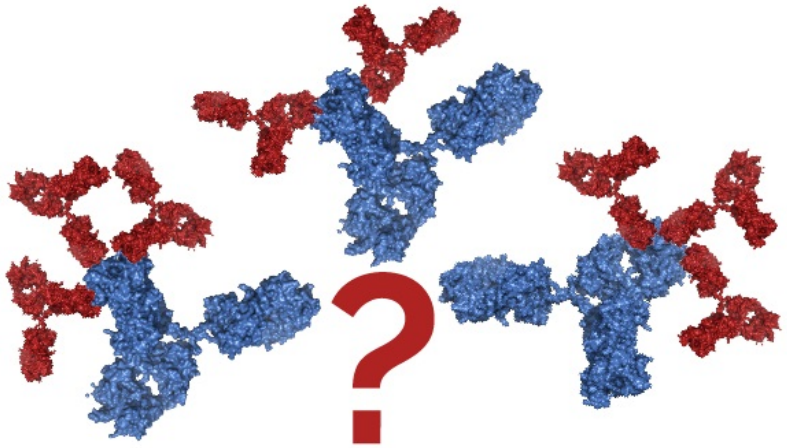
The Antibody Society

- We are an international non-profit representing individuals and organizations involved in antibody R&D and related fields
- Our initiatives are intended to broadly benefit our members and the scientific community, e.g.,
  - Antibody tool validation webinars
    - **Moderator: Dr. Simon Goodman**
  - Antibody therapeutics development metrics
  - Standards for next-generation sequencing data (Adaptive Immune Receptor Repertoire Community)
- We also educate, publish research results and contribute scientific content to numerous antibody-related conferences

The Antibody Society presents:



Antibody Validation Webinar Series

- On Demand
  - #1: Antibody specificity? What's the problem. Professor Andreas Plückthun
  - #2: Antibodies drive irreproducibility. Professor Glenn Begley and Professor Cecilia Williams
- Webinars Dec 4th, 5th 2019
  - #3: What's in a name? Finding the antibody for the job. Dr. Jan Voskuil and Professor Andy Chalmers
  - #4: What is this antibody? Professor Anita Bandrowski and Dr. Jan Voskuil
- More to come in 2020!

Access content via our Learning Center: www.antibodysociety.org/learningcenter

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Agenda

- Antibodies to watch in 2020*
  - Antibody therapeutics approved in the US or EU in 2019
    - 5 in total
  - Antibody therapeutics in regulatory review
    - 12 in total
  - Potential BLA/MAA submissions in 2019 or 2020
    - 17 in total

*Manuscript in preparation; anticipate posting on mAbs website in mid-December 2019

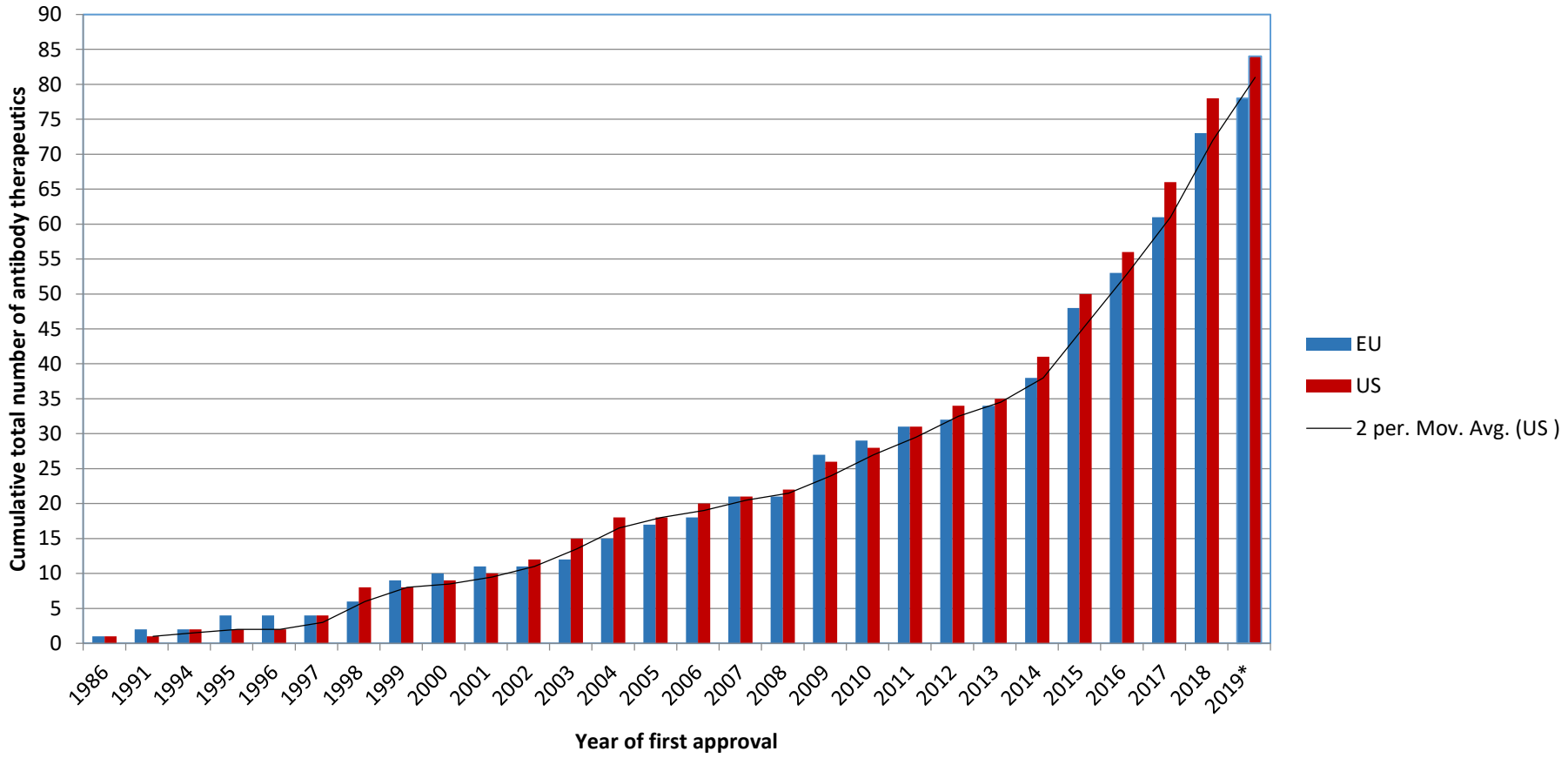
2019 approvals

- First approval in either the US or EU
  - Romosozumab (Evenity): approved in US
    - Anti-sclerostin IgG2 for osteoporosis
  - Risankizumab (Skyrizi): approved in both US and EU
    - Anti-IL-23p19 IgG1 for plaque psoriasis
  - Polatuzumab vedotin (Polivy): approved in US, review in EU
    - Anti-CD79b ADC for diffuse large B cell lymphoma
  - Brolucizumab (BEOVU): approved in US, review in EU
    - Anti-VEGF scFv for neovascular age-related macular degeneration
  - Crizanlizumab (Adakveo): approved in US, review in EU
    - Anti-P-selectin IgG2 for treatment to reduce the frequency of vaso-occlusive crisis

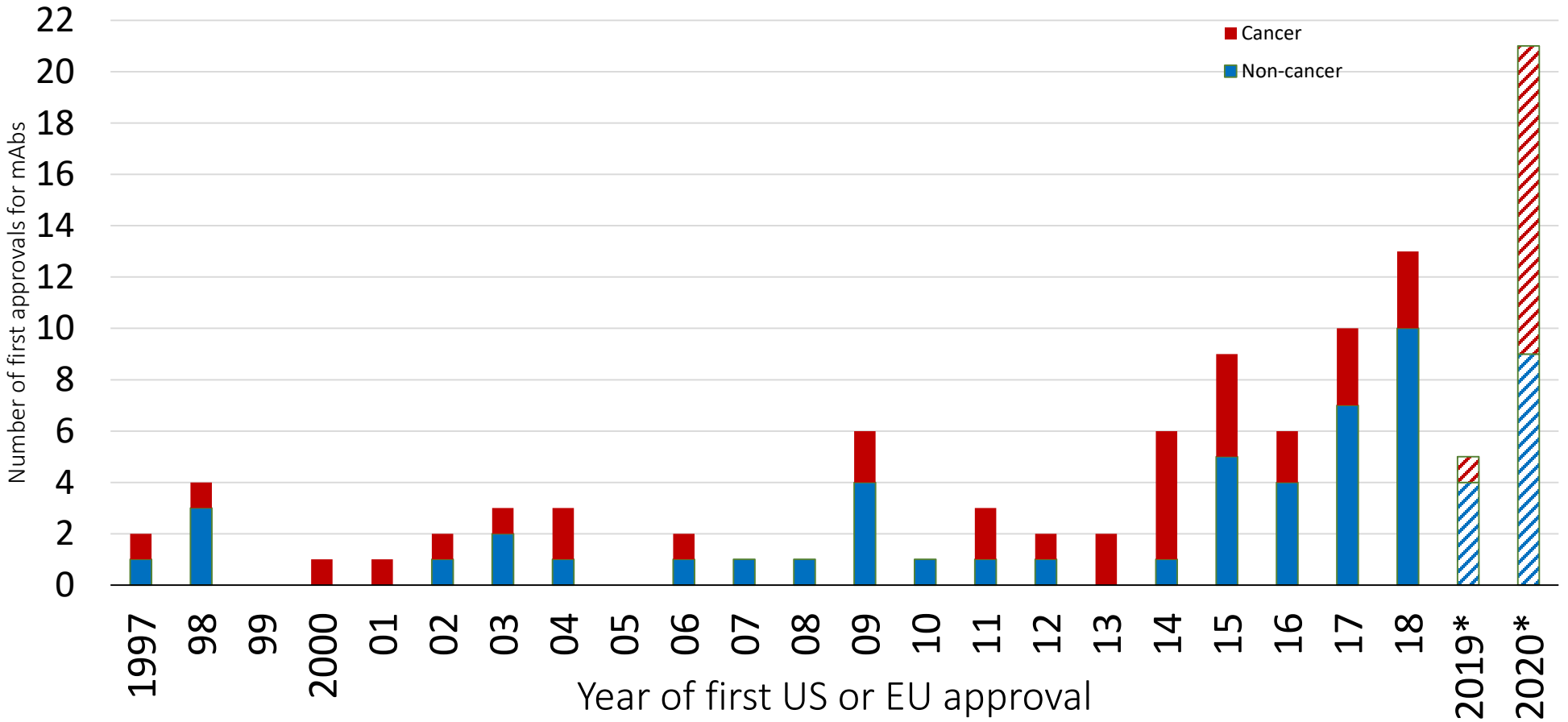
2019 approvals

- Notable other approvals
  - Netakimab: approved in Russia
    - Anti-IL-17 IgG1 for plaque psoriasis
    - BIOCAD has indicated that they will pursue approval in the EU
  - RabiMabs (trademarked as Twinrab): approved in India
    - Equipotent mixture of 2 murine mAbs targeting rabies virus glycoprotein for post-exposure prophylaxis in combination with rabies vaccine

Cumulative total: Approvals in EU & US



Annual first approvals in either the US or EU



*Estimate as of Nov 2019. 2020 estimate based on projected timing of BLA submissions and potential for priority review, and assumes approval on the first cycle.

Tables of approved mAbs and antibodies in review available at https://www.antibodysociety.org/resources/approved-antibodies/

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Antibodies to watch in 2020: US and EU regulatory review (12!)

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US or EU review: Non-cancer indications

- Eptinezumab: anti-CGRP IgG1 for migraine prevention
  - US review; February 21, 2020 PDUFA date
- Teprotumumab: anti-IGF-1R mAb for thyroid eye disease
  - US review; March 8, 2020 PDUFA date; Breakthrough Therapy, Orphan Drug and Fast Track designations
- Inebilizumab: anti-CD19, neuromyelitis optica spectrum disorder
  - US review, Breakthrough Therapy designation
- Satralizumab: anti-IL-6R for NMOSD
  - US and EU review; accelerated assessment in EU

US or EU review: Non-cancer indications

- Leronlimab: anti-CCR5 IgG4 for HIV infection
  - US review; Fast Track designation
- 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, accelerated approval possible
  - Omeros Corp. started rolling BLA in Oct 2019
- REGN-EB3: mixture of 3 IgG1 mAbs for Ebola virus infection
  - US review; Breakthrough Therapy designation
  - Regeneron has started rolling BLA

US or EU review: Cancer indications

- Isatuximab: anti-CD38 IgG1 for multiple myeloma
  - US and EU review
  - PDUFA date April 30, 2020
- Enfortumab vedotin: anti-Nectin-4 ADC for urothelial cancer
  - US review; PDUFA date March 15, 2020
- Sacituzumab govitecan: anti-TROP-2 ADC for triple-neg. breast cancer
  - US review; complete response letter sent in January 2019
  - Issues were focused on chemistry, manufacturing and control matters, and no new clinical or preclinical data was requested
- [fam-] trastuzumab deruxtecan: ant-HER2 ADC for breast cancer
  - US (Priority) and EU review; US Breakthrough Therapy, Fast Track designations
  - MHLW review (Japan)
- Tafasitamab (MOR208): anti-CD19 IgG1 for diffuse large BCL
  - US review; Breakthrough Therapy, Fast Track designations; Orphan Drug in US & EU
  - Morphosys started rolling BLA in Oct 2019

Antibodies to watch in 2020: Potential BLA/MAA submissions (17!)

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7 potential BLA submissions: H2 2019 (p.1)

- Belantamab mafodotin (GSK2857916): anti-BCMA IgG1 ADC for multiple myeloma
  - Breakthrough Therapy (US) and PRIME (EU) designations
  - GSK has pivotal data to support its filing by the end of the year
- Oportuzumab monatox (Vicinium®): anti-EpCAM scFv immunotoxin for bladder cancer
  - Fast Track designation; FDA aligned with use of Accelerated Approval pathway with rolling review
  - Sesen Bio expects to initiate submission of BLA in Q4 2019
- Spartalizumab (PDR001): anti-PD-1 IgG4 for melanoma
  - Novartis expects to submit marketing application(s) in 2019
- Dostarlimab (TSR-042): anti-PD-1 IgG4 for recurrent MSI-H tumors
  - GSK, AnaptysBio anticipate a BLA submission in H2 2019

Potential BLA submissions H2 2019 (p.2)

- Margetuximab: anti-HER2 IgG1 mAb for breast cancer
  - Fast Track designation
  - MacroGenics anticipates submitting a BLA in Q4 2019
- Omburtamab: anti-B7-H3 (CD276) murine IgG1 for neuroblastoma
  - Rare Pediatric Disease, Breakthrough Therapy, Orphan designations
  - Y-mAbs Therapeutics expects to submit a BLA in 2019
- Naxitamab: anti-GD2 IgG1 for neuroblastoma
  - Rare Pediatric Disease, Breakthrough Therapy, Orphan designations
  - Y-mAbs Therapeutics expects to start rolling BLA in Nov. 2019

2 potential BLA submissions: H1 2020

- Tanezumab: anti-NGF IgG2 for osteoarthritis pain
  - Fast Track designation
  - Pfizer/Lilly plan BLA submission by Q1 2020
- Aducanumab: anti-amyloid β IgG1 for early Alzheimer's disease
  - Fast Track designation; PRIME designation
  - Biogen/Eisai plan to submit BLA in early 2020

8 other potential 2020 BLA submissions (p.1)

- Sutimlimab: anti-C1s IgG4 for cold agglutinin disease
  - Breakthrough Therapy designation
  - Sanofi in planning regulatory submissions in 2020
- Evinacumab: anti-angiopoietin-like protein 3 IgG4 for hypercholesterolemia
  - Breakthrough Therapy designation
  - Regeneron may submit data to regulatory agencies in 2020
- Anifrolumab: anti-type 1 IF-R IgG1 for lupus
  - Fast Track designation
  - AstraZeneca anticipates regulatory submission(s) in 2020
- Teplizumab (PRV-031): anti-CD3 IgG1 for type 1 diabetes
  - Breakthrough Therapy designation, PRIME designation
  - Provention Bio will meet w/ FDA in Q4 2019; possible Q4 2020 submission
- Etrolizumab: anti-integrin (β7 subunit) IgG1 for ulcerative colitis
  - Roche anticipates regulatory submissions in 2020

Other potential 2020 BLA submissions (p.2)

- Loncastuximab tesirine (ADCT-402): anti-CD19 IgG1 ADC for diffuse large B-cell lymphoma
  - ADC Therapeutics SA intends to submit a BLA in H2 2020
- Balstilimab (AGEN2034): anti-PD-1 IgG4 for cervical cancer
  - Monotherapy
- Zalifrelimab (AGEN1884): anti-CTLA4 IgG1 for cervical cancer
  - Studies being done in combination with AGEN2034
  - Agenus may submit BLA as early as 2020 seeking accelerated approval if study results are positive

Antibodies to watch in 2021 and beyond

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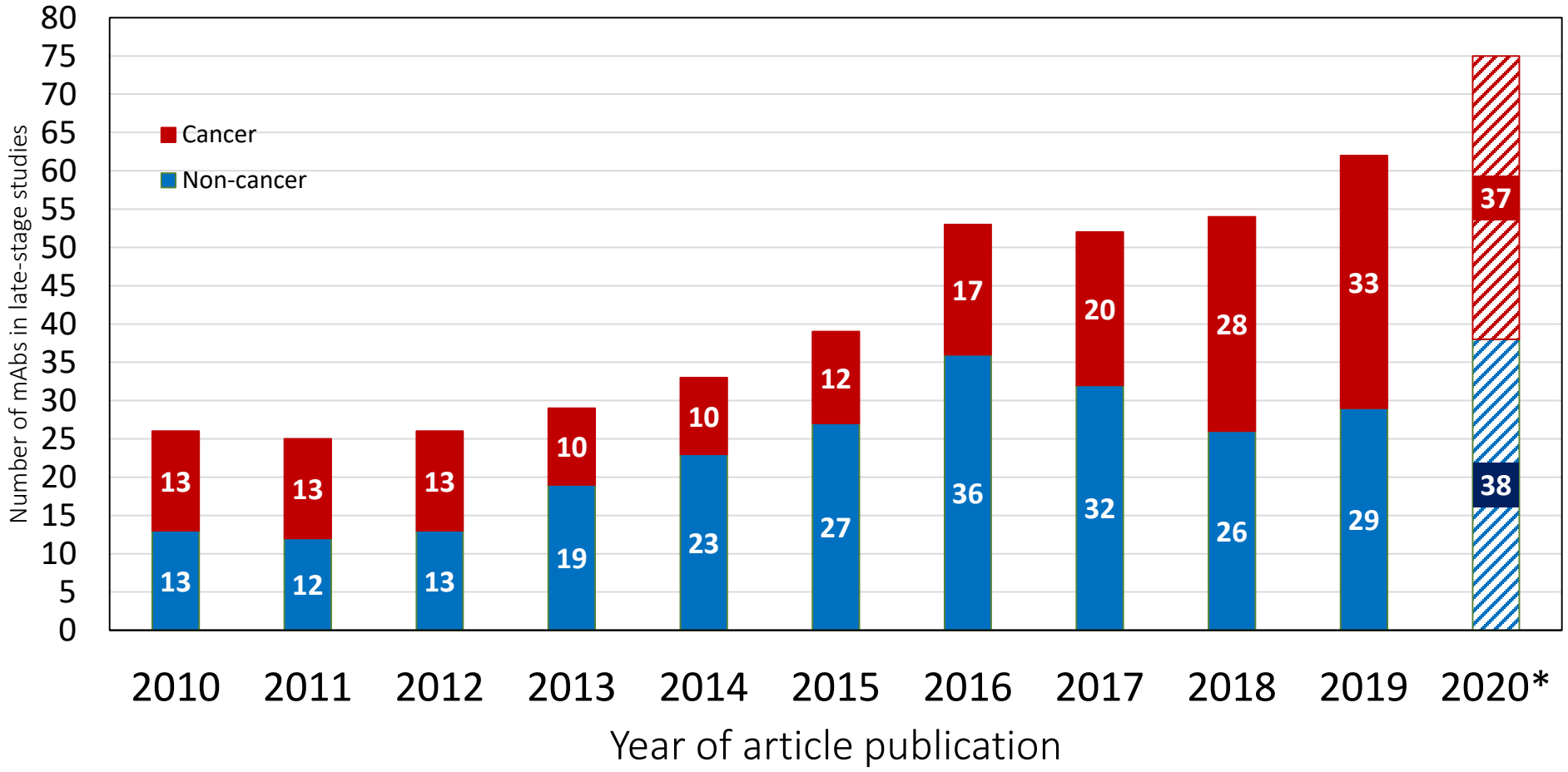
Antibodies in late-stage studies



* 2020 data as of Nov 12, 2019. Data from 'Antibodies to watch' articles published in *mAbs, e.g.,* Kaplon H & Reichert JM. Antibodies to watch in 2019. mAbs (doi.org/10.1080/19420862.2018.1556465). Table of antibodies in late-stage studies available at antibodysociety.org

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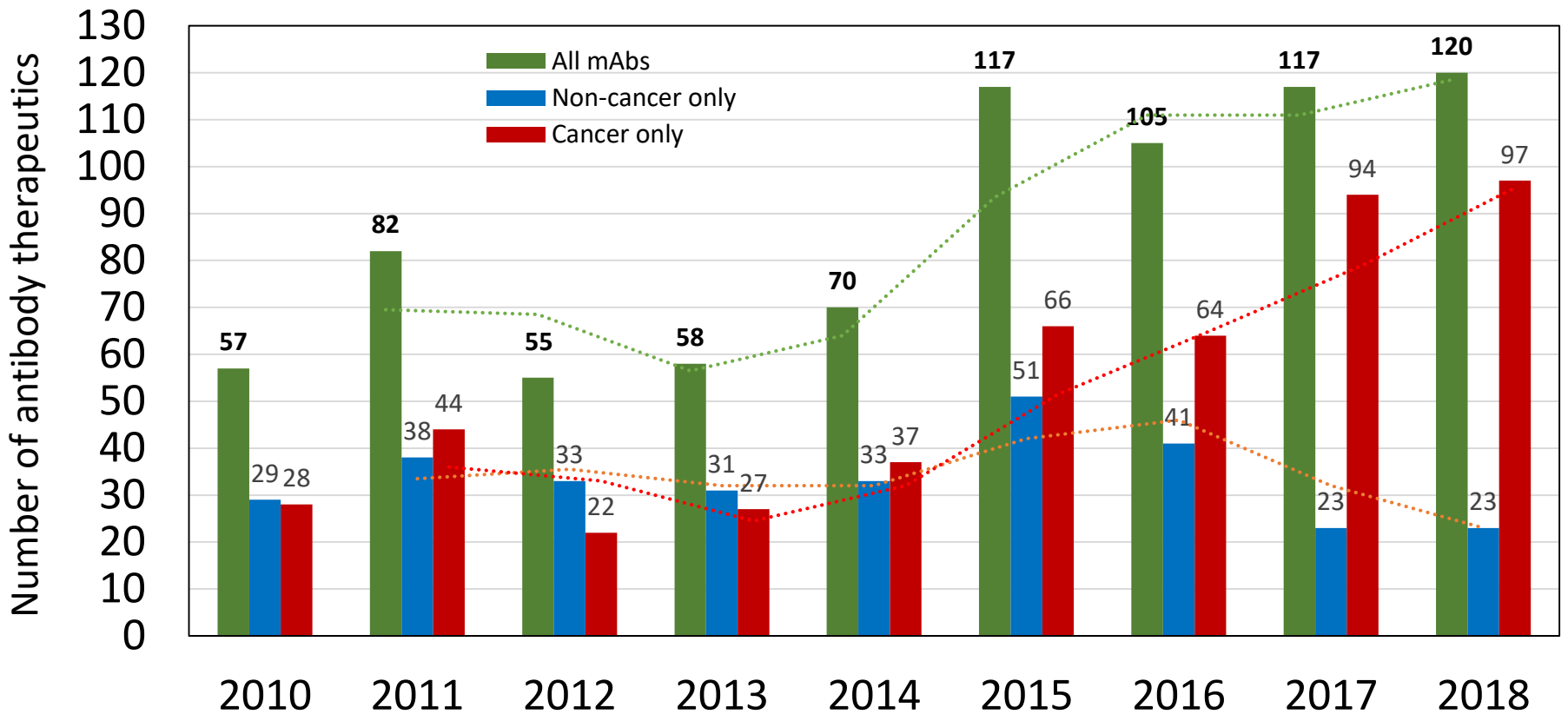
Antibodies starting first clinical studies



Totals include mAbs sponsored by commercial firms only; dotted lines are 2-yr moving ave.

Source: The Antibody Society. Table of antibodies in early-stage studies available at antibodysociety.org

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Key messages

- 2019 has been a slow year for first approvals of antibody therapeutics in the US and EU, but projections indicate that 2020 will be much better
  - Refined data will be available in the “Antibodies to watch in 2020” paper, to be posted on mAbs website in December 2019
- Rate of entry into first clinical studies for antibody therapeutics continues to be high, with cancer currently the preferred therapeutic area
  - Immune checkpoint modulators and bispecifics are the preferred types
  - For more on bispecifics, see tables in: Labrijn AF, Janmaat ML, Reichert JM, Parren PWHI. Bispecific antibodies: a mechanistic review of the pipeline. Nat Rev Drug Discov. 2019 Aug;18(8):585-608.

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Thanks for attending!

Janice M. Reichert, Ph.D.
Executive Director, The Antibody Society
janice.reichert@antibodysociety.org

Please join us!

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www.antibodysociety.org

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Society member benefits

- Access to valuable antibody therapeutics pipeline data and other content in the **Members Only** section of the website
- Discounted registration for our annual meeting, Antibody Engineering & Therapeutics
- Discounts of up to 20% on registration for other antibody-relevant meetings
- Access to research and educational resources provided by the Society
- Opportunities to participate in the Society's initiatives
- Opportunities to network with Society members

Membership is free for students, post-docs, AIRR Community meetings attendees and all employees of our corporate sponsors.