“Antibodies to watch” and more: Early- and late-stage clinical development trends

KNect365’s Digital Week, June 26, 2019

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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
- Benefits of membership include:
  - 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

Agenda

- Antibodies to watch in 2019 update
  - Antibody therapeutics approved in the US or EU in 2019 (as of June 2019)
  - Antibody therapeutics in regulatory review
  - Potential BLA/MAA submissions in 2019, leading to 2020 approvals
- Antibodies that entered clinical studies recently
  - Summary for 2018-June 2019
  - Trends in format and mechanism of action
  - Popular and less trendy targets

Antibodies to watch in 2019 and 2020

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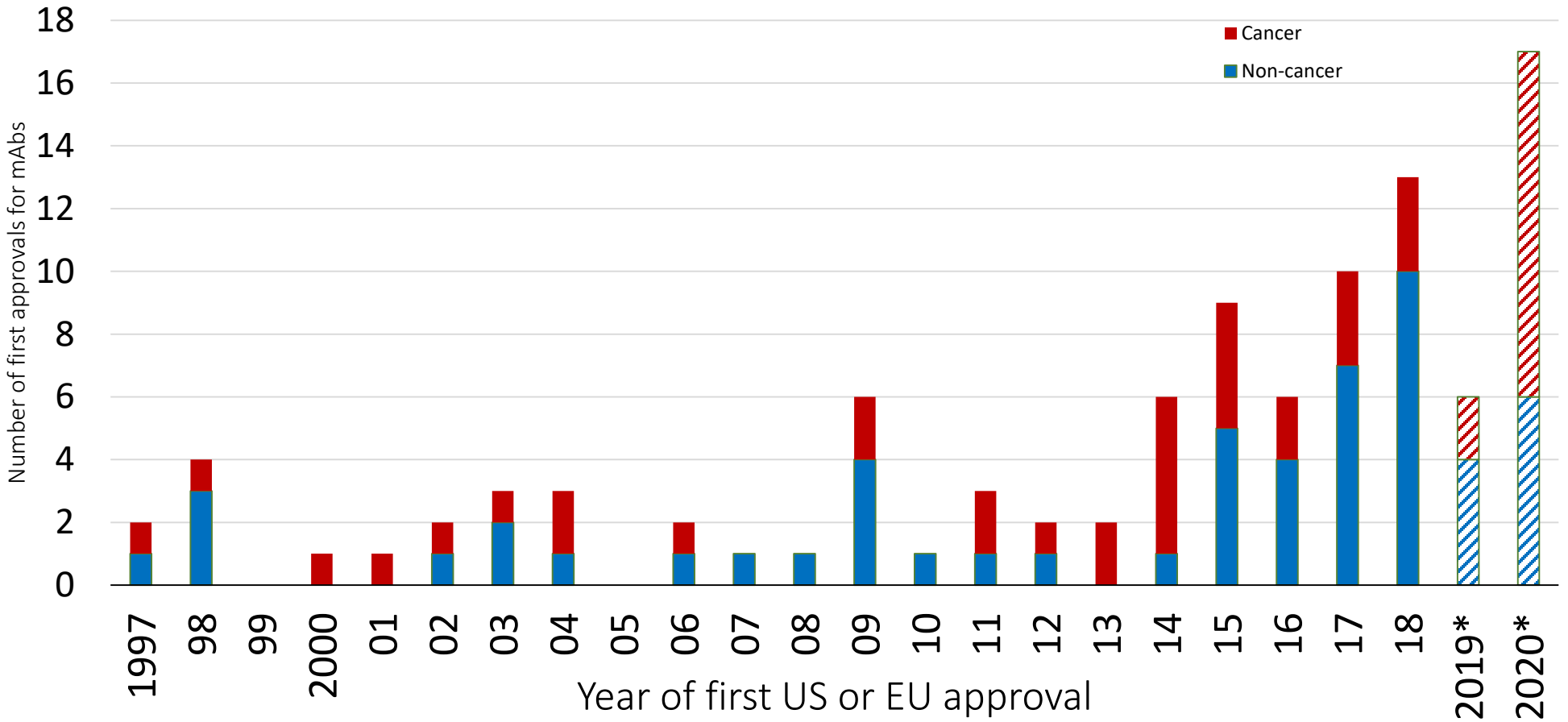
2019 approvals (as of June 10)

- First approval in either the US or EU
  - Romosozumab: approved in US, review in EU. First approved in Japan in Jan.
    - Anti-sclerostin IgG2 for osteoporosis
  - Risankizumab: approved in both US and EU
    - Anti-IL-23p19 IgG1 for plaque psoriasis
  - Polatuzumab vedotin: approved in US, review in EU
    - Anti-CD79b ADC for diffuse large B cell lymphoma
- Also approved in the US or EU in 2019
  - Caplacizumab: approved in the US (2018 EU approval)
    - Anti-von Willebrand factor nanobody for acquired thrombotic thrombocytopenic purpura
  - Fremanezumab: approved in the EU (2018 US approval)
    - Anti-CGRP IgG2 for migraine prevention
- Notable other approvals
  - Netakimab: approved in Russia
    - Anti-IL-17 IgG1 for plaque psoriasis

US or EU review: Possible 2019 approvals

- Brolucizumab: anti-VEGF-A scFv for macular degeneration
  - Priority review in US, launch in US anticipated by year end; also in EU review
- Leronlimab: anti-CCR5 IgG4 for HIV infection
  - US review; Fast track designation
- Isatuximab: anti-CD38 IgG1 for multiple myeloma
  - US and EU review

Annual first approvals in either the US or EU



*Estimate as of June 2019.

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

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In US or EU review, but unlikely for 2019

- Eptinezumab: anti-CGRP IgG1 for migraine prevention
  - US review; PDUFA date is February 21, 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

Potential mid-2019 BLA submissions

- Teprotumumab: anti-IGF-1R mAb for thyroid eye disease
  - Horizon Therapeutics expects to submit a BLA to FDA in mid-2019
  - FDA Breakthrough Therapy, Orphan Drug and Fast Track designations
- Inebilizumab: anti-CD19, neuromyelitis optica spectrum disorder
  - Viela Bio expects to submit a BLA with the FDA in mid-2019

Potential 2019 BLA submissions H2 2019 (1)

- Trastuzumab deruxtecan: anti-HER2 ADC for breast cancer
  - AZ and Daiichi Sankyo anticipate a BLA submission in H2 2019
- Enfortumab vedotin: anti-Nectin-4 ADC for urothelial cancer
  - Seattle Genetics and Astellas plan to submit BLA this year
- Belantamab mafodotin (GSK2857916): anti-BCMA IgG1 for multiple myeloma
  - Breakthrough Therapy (US) and PRIME (EU) designations
  - GSK plans to have pivotal data to support its filing by the end of the year
- Oportuzumab monatox (Vicinium®): anti-EpCAM immunotoxin for bladder cancer
  - 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 for melanoma
  - Novartis expects to submit marketing application(s) in 2019
- Dostarlimab (TSR-042): anti-PD-1 for recurrent MSI-H tumors
  - GSK, AnaptysBio anticipate a BLA submission in H2 2019

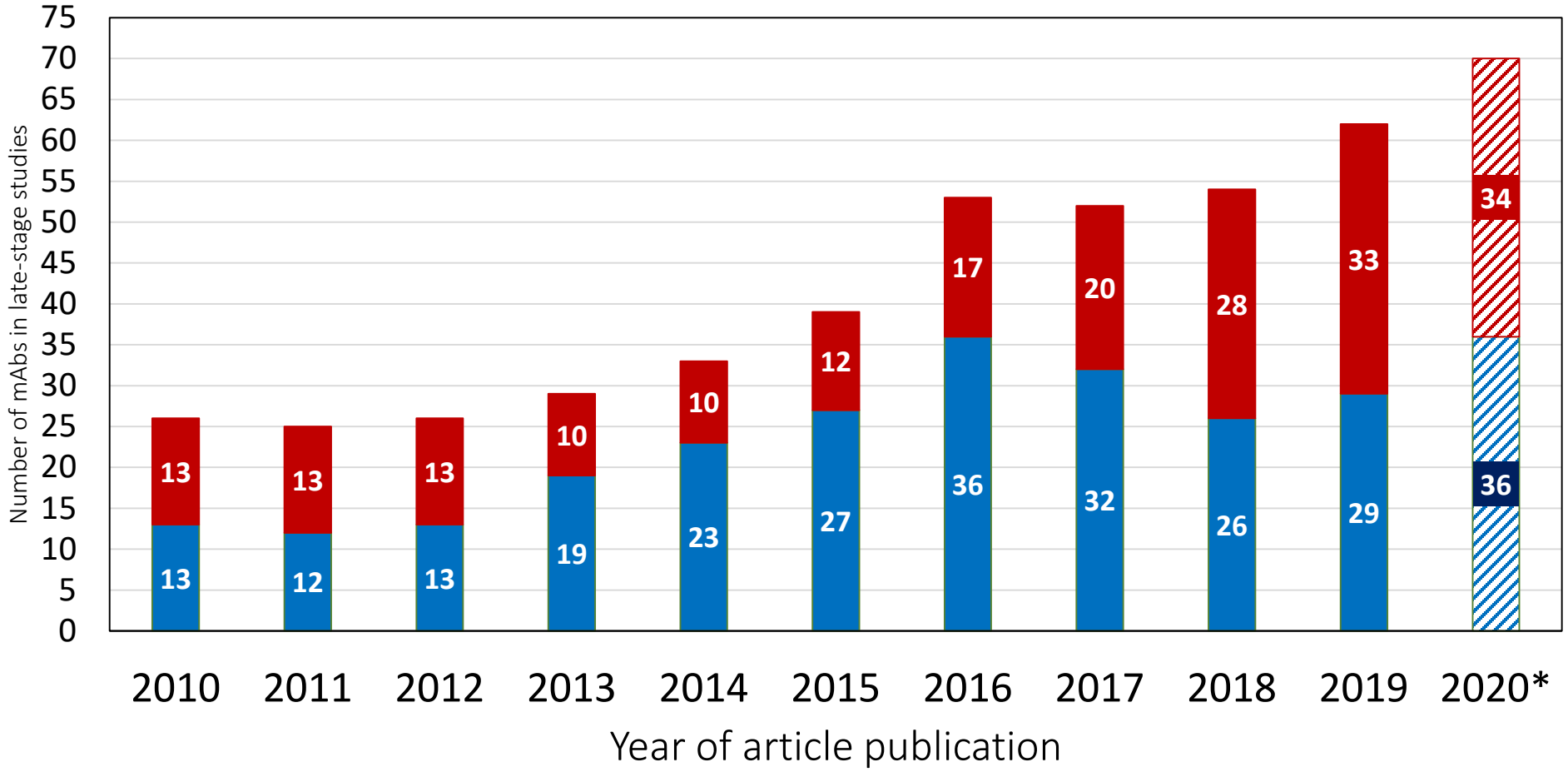
Potential 2019 BLA submissions H2 2019 (2)

- Tafasitamab (MOR208): anti-CD19 mAb for diffuse large BCL
  - Morphosys plans to file a BLA application for MOR208 in Q4 2019
- Margetuximab: anti-HER2 IgG1 mAb for breast cancer
  - MacroGenics anticipates submitting a BLA in H2 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 submit a BLA in 2019

Potential 2019 BLA submissions H2 2019 (3)

- Crizanlizumab: anti-CD62 (aka P-selectin) for sickle cell disease
  - Novartis expects to submit marketing application(s) in 2019
- Narsoplimab: anti-mannan-binding lectin-associated serine protease-2 (MASP-2) mAb for hematopoietic stem cell transplant-associated thrombotic microangiopathy
  - Omeros Corp. preparing BLA and MAA; EMA has appointed rapporteurs and FDA agreed to rolling BLA and possibility of accelerated approval
- Satralizumab: anti-IL-6R for NMOSD
  - Listed in Roche pipeline as a 2019 NME submission

Antibodies in late-stage studies



* 2020 data as of June 2019, incl. Phase 3 studies listed as not yet recruiting on clinicaltrials.gov. 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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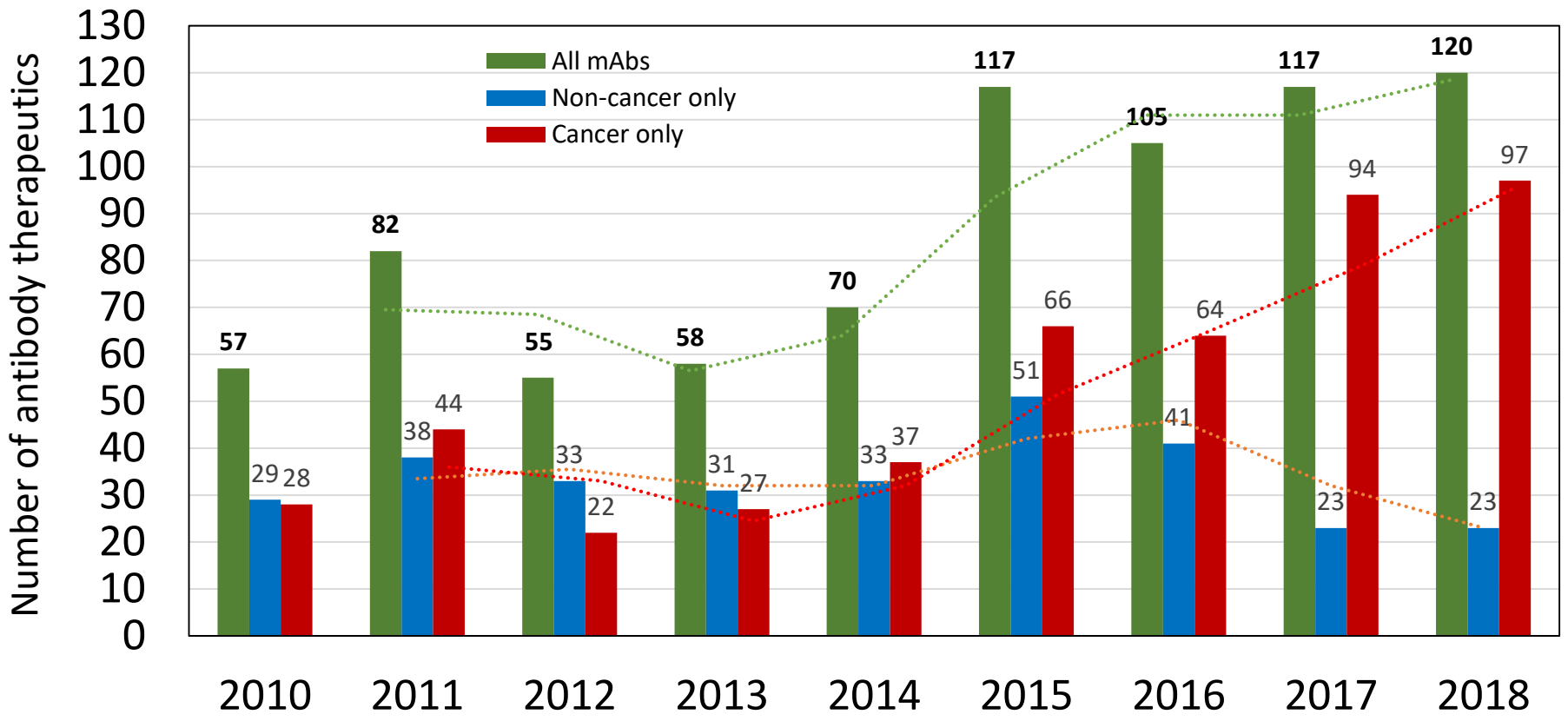
Antibodies that recently entered clinical study

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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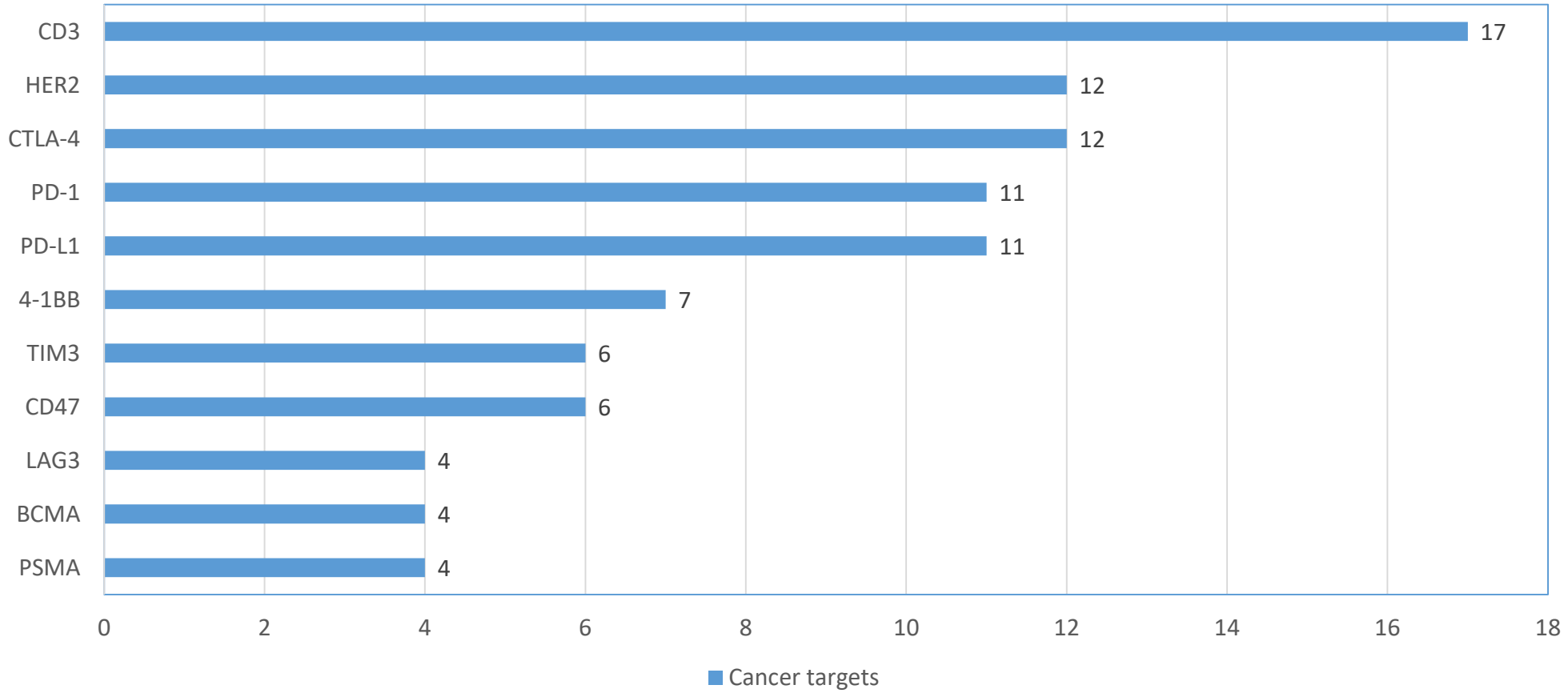
2018 to mid-2019 first clinical studies

- Therapeutic areas, formats and mechanisms of action for antibody therapeutics entering clinical study during Jan 1, 2018 to June 1, 2019:
  - 159 mAbs in total
  - 128 (80% of the total) are in studies of patients with cancer
  - 31 (20% of the total) are in studies of patients with non-cancer indications
  - 61 (38% of the total) are immune checkpoint modulators
  - 48 bispecifics* (30% of the total)
    - 17 (11% of total) are T cell engagers
  - 25 ADCs (16% of the total)

For a recent review of bispecific mAbs, see Labrijn et al. Bispecific antibodies: a mechanistic review of the pipeline. Nat Rev Drug Discov. 2019 Jun 7. doi: 10.1038/s41573-019-0028-1

Frequent* cancer targets for recent entrants



*Total number of mAbs = 128. If the targets in a bispecific are different, each is included in the totals

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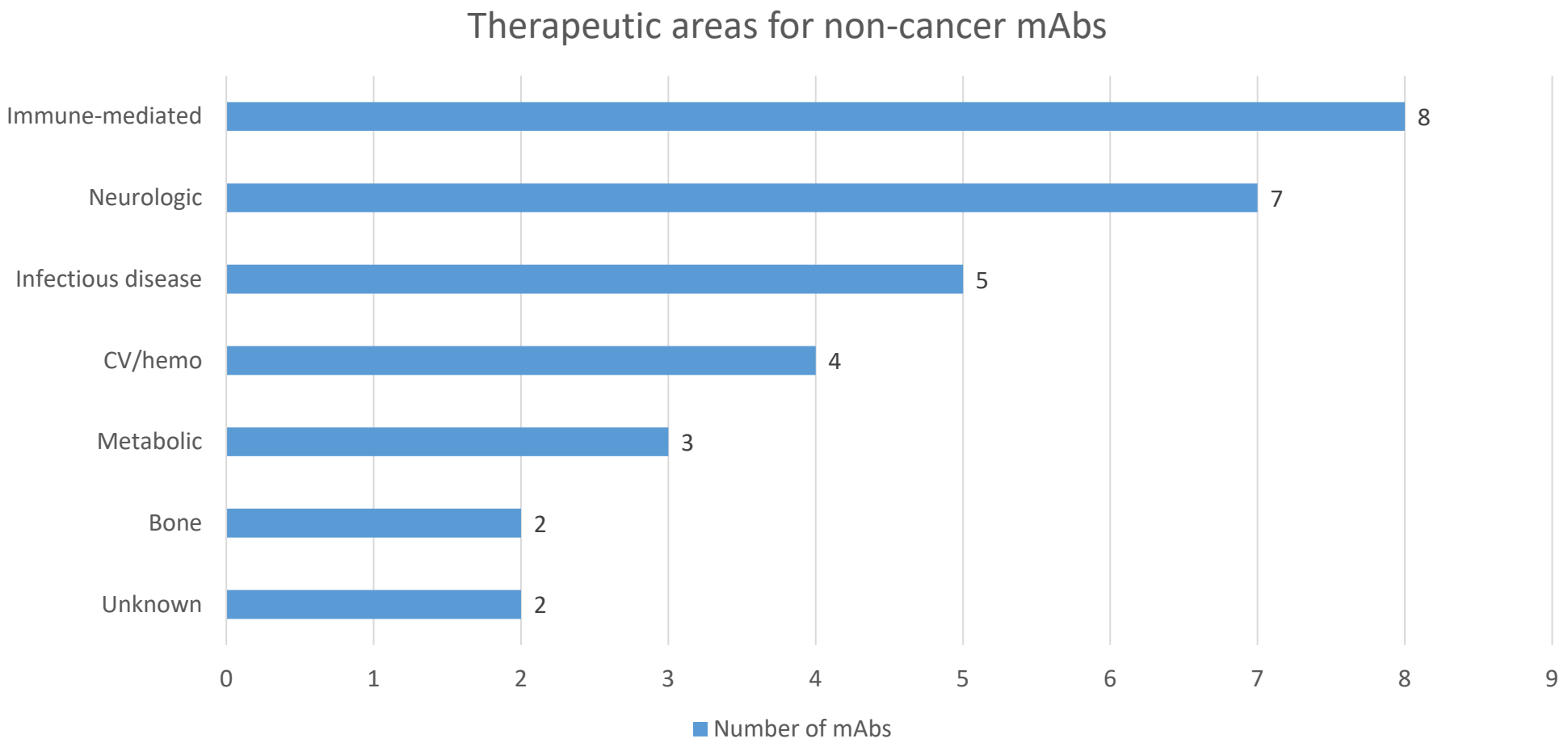
Focus on anti-HER2 mAbs

- All 12 anti-HER2 mAbs are enhanced in some way:
  - 5 are antibody-drug conjugates (drugs include MMAE, MMAF, PDB-MA)
  - 1 is a bispecific (biparatopic) ADC
  - 4 are bispecific mAbs
    - 3 are biparatopic
    - 1 is a T-cell engager
  - 1 is an immunotoxin (mAb conjugated to Shiga-like toxin)
  - 1 is an immune stimulator antibody conjugate (mAb conjugated to TLR7 agonist)

Less trendy cancer targets

- Of the 128 anti-cancer mAbs, unique targets are:
  - C5aR
  - CD39
  - CD46
  - CD48/Signaling Lymphocyte Activation Molecule family member 2 (SLAMF2)
  - CD74
  - Clever-1
  - ILDR2
  - Leucine-rich repeat containing 32 (LRRC32)/ glycoprotein A repetitions predominant (GARP)
  - Leukemia inhibitory factor
  - MUC16 (and CD3)
  - NRP1
  - PVRIG
  - ROR2
  - Somatostatin receptor 2 (and CD3)

31 mAbs for non-cancer indications



Note: mAbs in “unknown” category are in Phase 1 studies of health volunteers

Key messages

- 2019 will be 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 discussed at Antibody Engineering & Therapeutics (December 2019 in San Diego)
- 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

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Thanks for attending!

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