**Supplementary information**

# Immuno-oncology clinical trials take a turn beyond PD1/PDL1 inhibitors

In the format provided by the authors
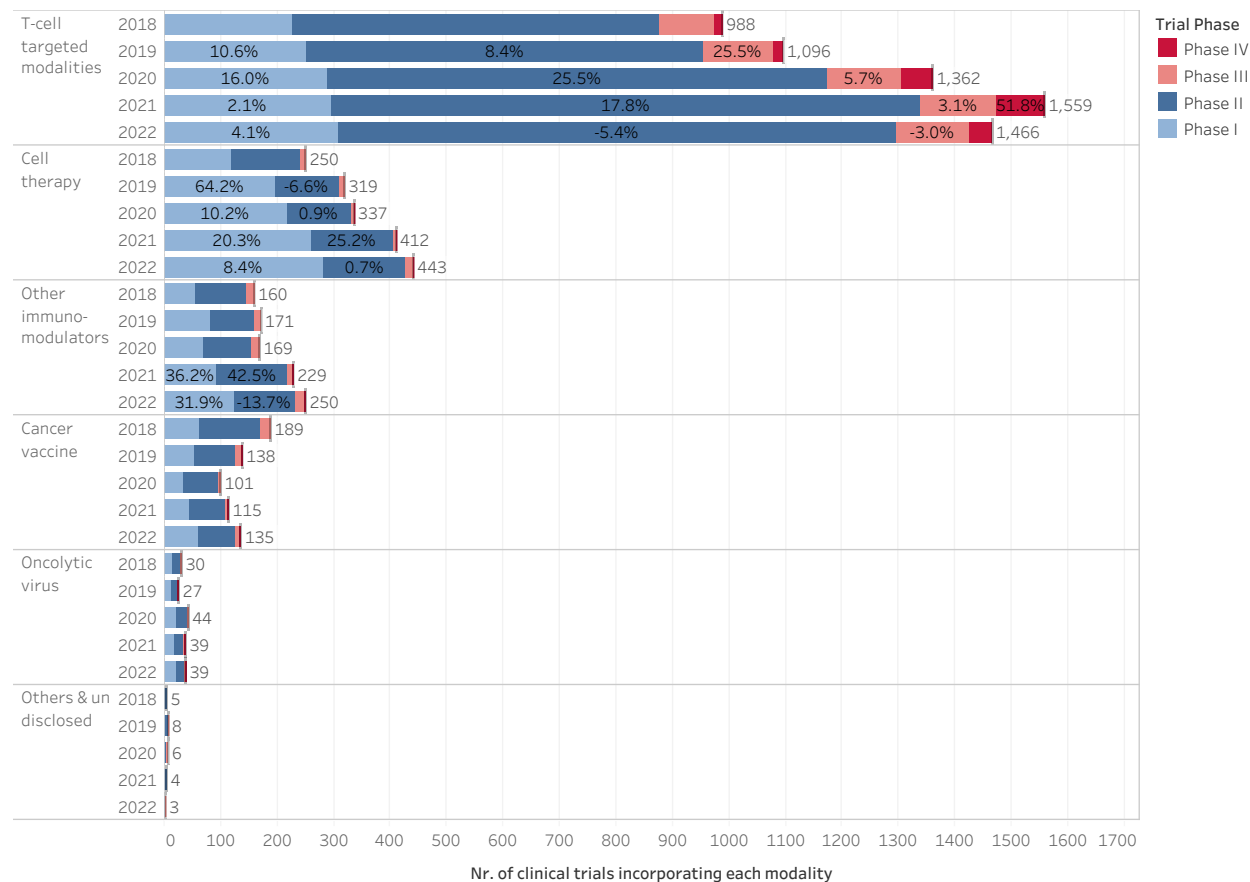
Supplementary figures

Supplementary Figure 1: Global landscape of IO clinical trials. (a) There are 17,558 IO clinical trials registered in CRI's database. Colours indicate trial status as of data cut-off (February 2023). (b) Number of trials by trial start date.
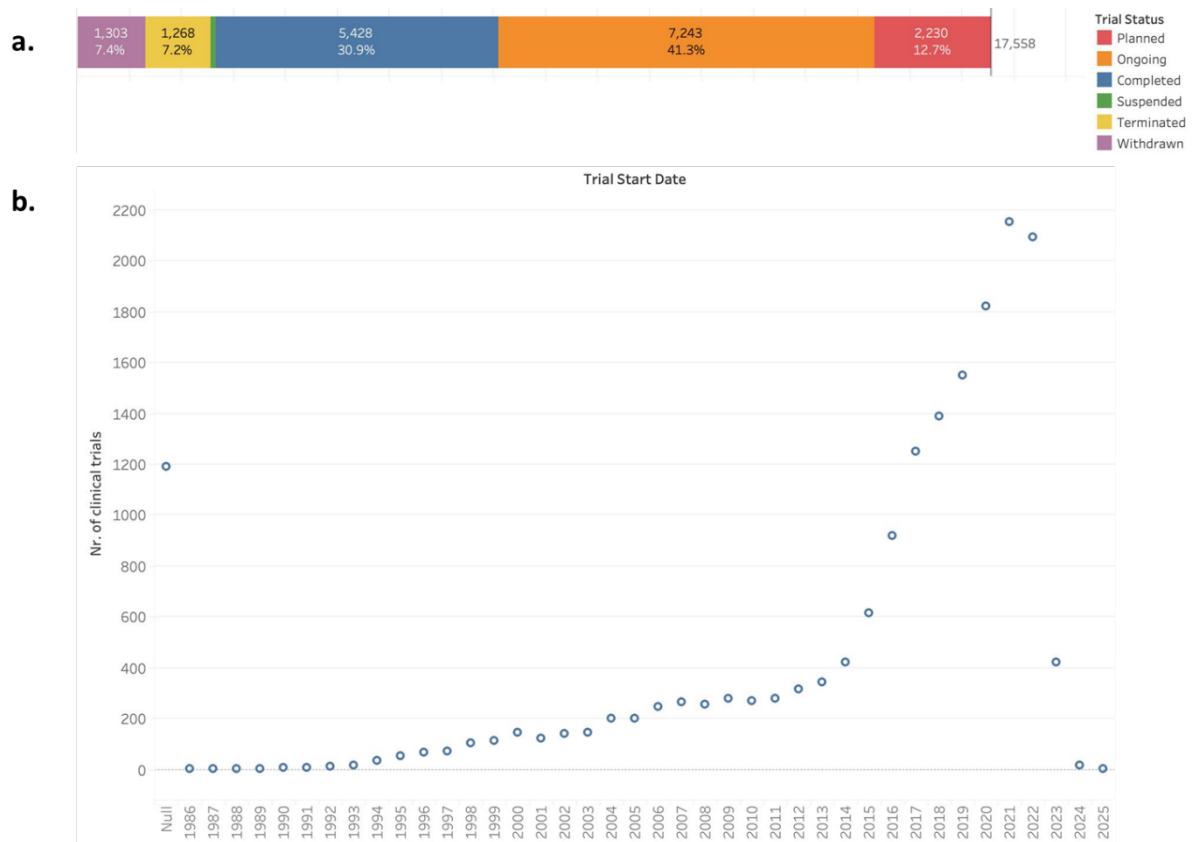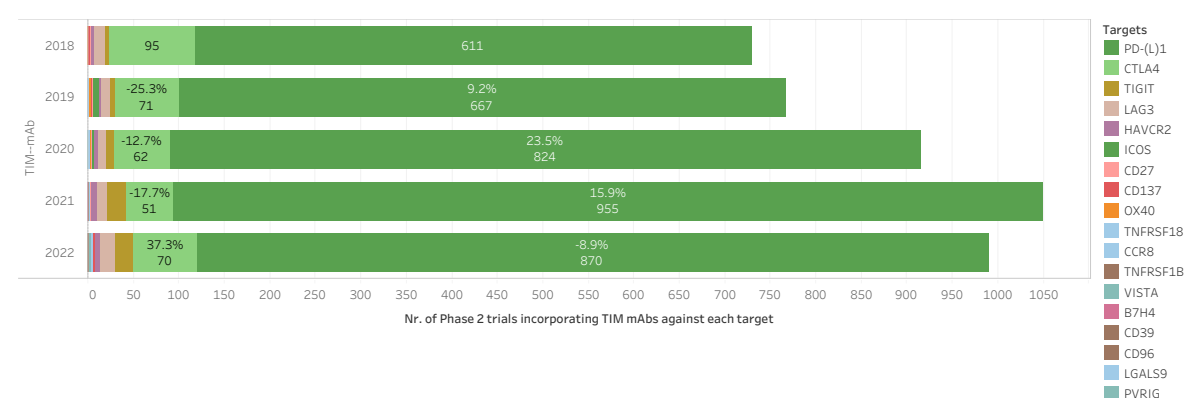
Supplementary Figure 2: IO trials by indication. (a) Number of clinical trials by indication and trial start date (2018 to 2022 only). (b) Number of clinical trials by indication, phase and start date (2020 to 2020 only). In both panels, % indicates year-over-year growth.
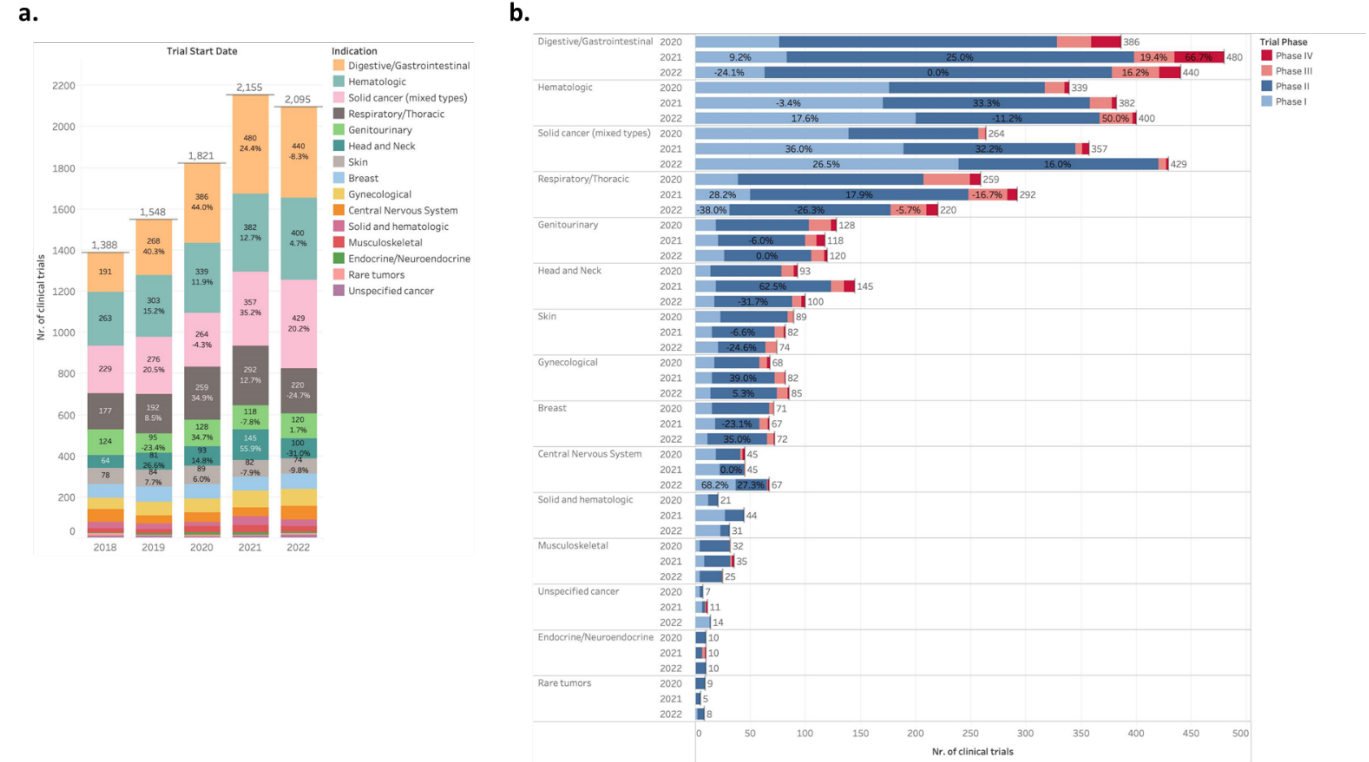
Supplementary Figure 3: IO drug modalities in oncology clinical trials. Number of clinical trials using each IO drug modality, by year of start and trial phase. Total number of trials in this figure does not correspond to number of unique trials (those trials assessing more than one IO modality will be counted once for each different IO modality assessed). % indicates year-over-year growth.
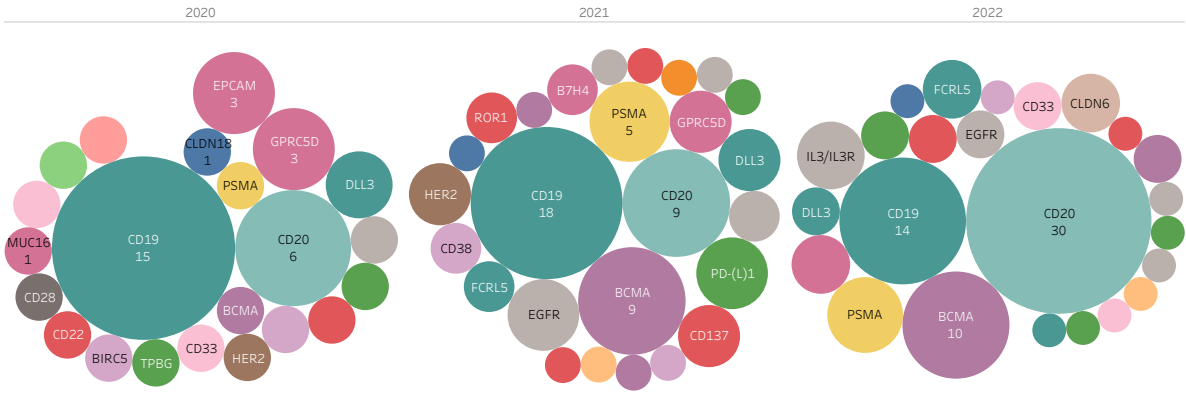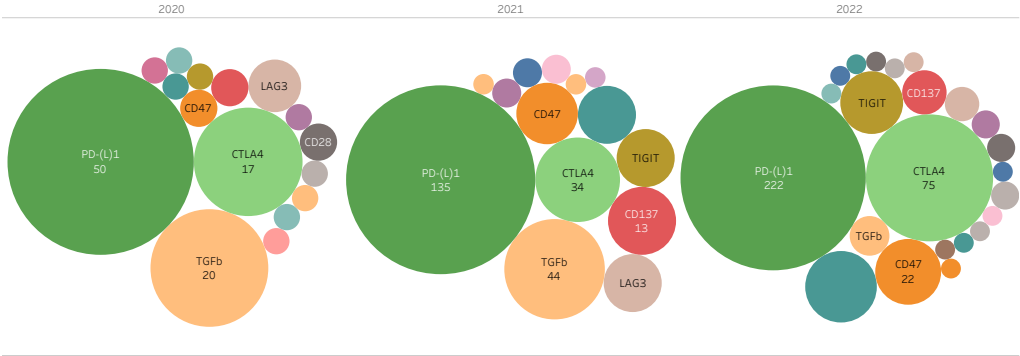
Supplementary Figure 4: T-cell immunomodulators (TIMs) in oncology clinical trials. (a) Number of clinical trials employing each TIM modality, by trial start year. Total number of trials in this figure does not correspond to number of unique trials (those trials assessing more than one TIM modality will be counted once for each different IO modality assessed). (b) Targets of T cell immunomodulator monoclonal antibodies (TIM mAbs) used in trials starting between 2020 and 2022. % indicates year-over-year growth. (c) Phase II trials incorporating TIM mAbs, by target. Total number of trials in this figure does not correspond to number of unique trials (those trials employing TIM mAbs against different targets will be counted once for each target).

a.

b.

c.

Supplementary Figure 5: Targets of other T-cell immunomodulators in oncology clinical trials. (a) Targets of T cell engagers used in trials starting between 2020 and 2022. (b) Targets of TIM bispecifics and multispecific antibodies employed in oncology trials starting between 2020 and 2022. In both panels, values indicate number of clinical trials.
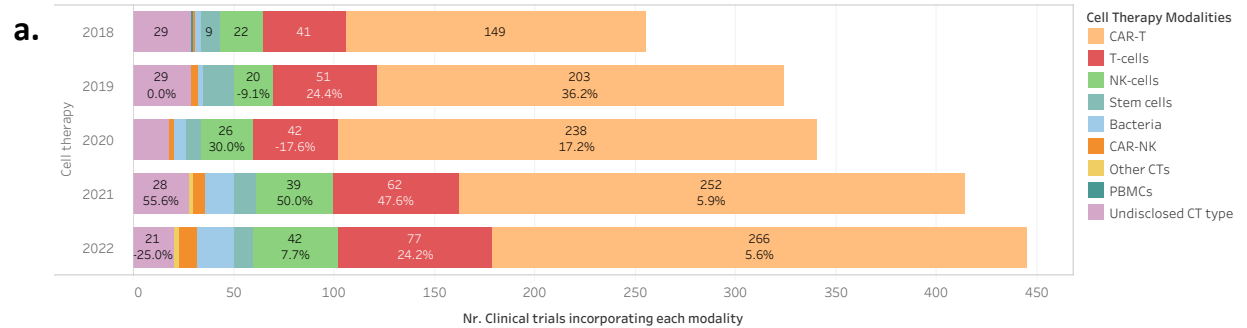
a. Targets of T-cell engagers

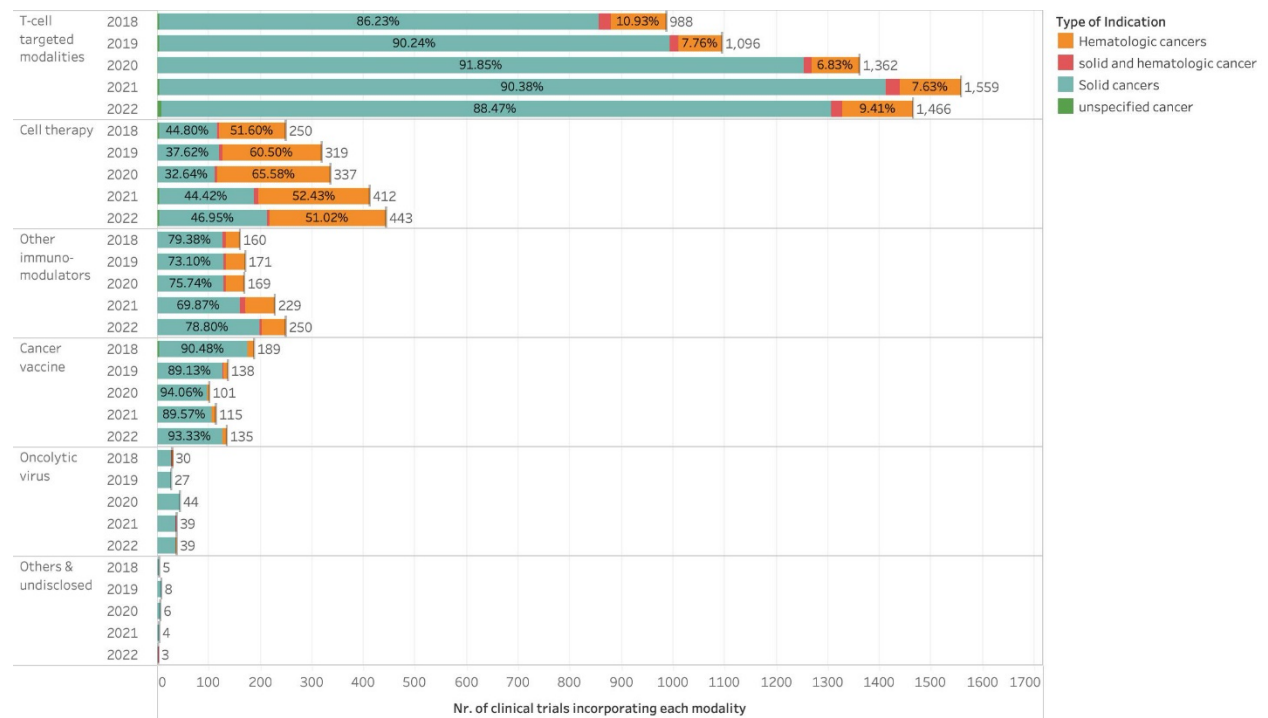**b.** Targets of other TIM bispecifics/ multispecifics

Supplementary Figure 6: Cell therapy modalities in oncology clinical trials. (a) Number of clinical trials evaluating each cell therapy modality, by trial start year. Total number of trials in this figure does not correspond to number of unique trials (those trials assessing more than one cell therapy modality will be counted once for each different cell therapy modality assessed). % indicates year-over-year growth. (b) Targets of cell therapies used in oncology trials starting between 2020 and 2022. Values indicate number of clinical trials.
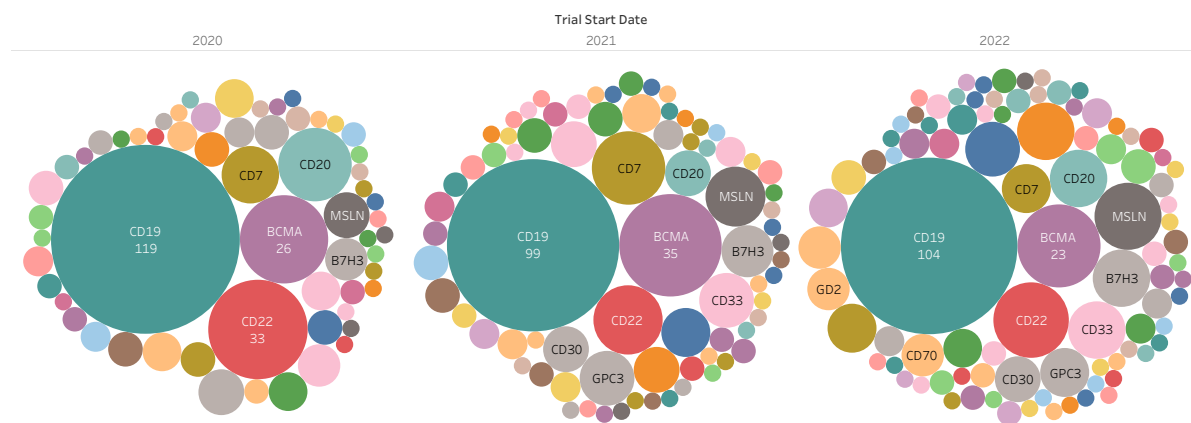
Supplementary Figure 7: IO drug modalities in oncology clinical trials by tumor type. Number of clinical trials employing each IO drug modality, by year of start and tumor type. Total number of trials in this figure does not correspond to number of unique trials (those trials employing more than one modality will be counted once for each different IO modality employed). % indicates percentage of total, per bar.
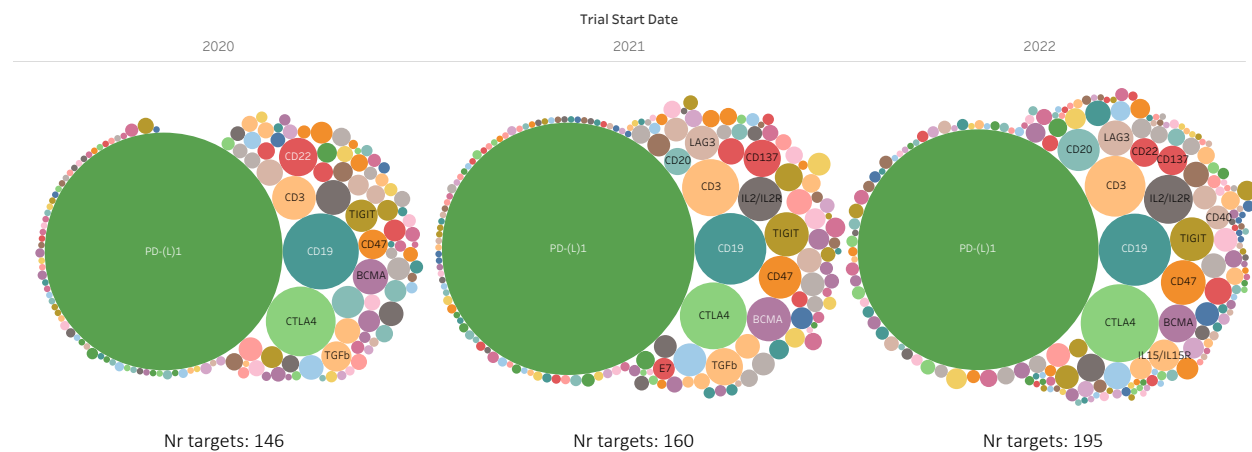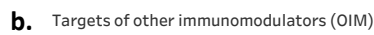
Supplementary Figure 8: Other immunomodulators (OIM) in oncology clinical trials . (a) Number of clinical trials assessing each OIM modality, by trial start year. Total number of trials in this figure does not correspond to number of unique trials (those trials assessing more than one OIM modality will be counted once for each different OIM modality used). % indicates year-over-year growth. (b) Targets of OIM drugs assessed in oncology trials starting between 2020 and 2022. Values indicate number of clinical trials.

Supplementary Figure 9: Target of IO drugs in oncology clinical trials. Full picture of targets of all IO drugs employed in oncology clinical trials starting between 2020 and 2022.

Supplementary Methods

<u>Dataset and analysis</u>

The data on immuno-oncology (IO) clinical trials were collected from GlobalData's Trial Database and subsequently curated by Cancer Research Institute (CRI) based on CRI IO Analytics definition of different immunotherapy types and drug target information. The data cut-off is February 2023.

IO therapies were classified into 6 main categories based on the different mechanisms of action: (1) Immunotherapies directed towards T cells ("T-cell-targeted immunotherapies" or "TIM"), (2) Immunotherapies targeted to cell types other than T cells ("Other immunotherapies" or "OIM"), (3) Cell therapies 4) Cancer vaccines (5) Oncolytic viruses and (6) other or undisclosed therapies. Larger categories have been further divided into subcategories attending to molecule type (TIM and OIM) or cell type (Cell therapies):

- TIM/OIM subcategories: (1) monoclonal antibody (mAb), (2) bispecific or multispecific antibody, (3) cell engager, (4) recombinant and/or fusion protein, (5) nucleotide, (6) small molecule and (7) others/undisclosed.
- Cell therapies: (1) CAR-T cells, (2) T-cells, (3) NK cells, (4) stem cells, (5) CAR-NK cells, (6) PBMCs, (7) Bacteria, (8) other cell therapies, (9) undisclosed cell therapies. Of note, dendritic cells and other antigen-presenting cells are not included in the Cell therapies category but in the Cancer Vaccines category.

Cancer types classification by body location/system was done following the National Cancer Institute guidelines: https://www.cancer.gov/types/by-body-location

Analyses and graphical representations were done by using Tableau.