CGP opening the possibilities of personalised healthcare in oncology

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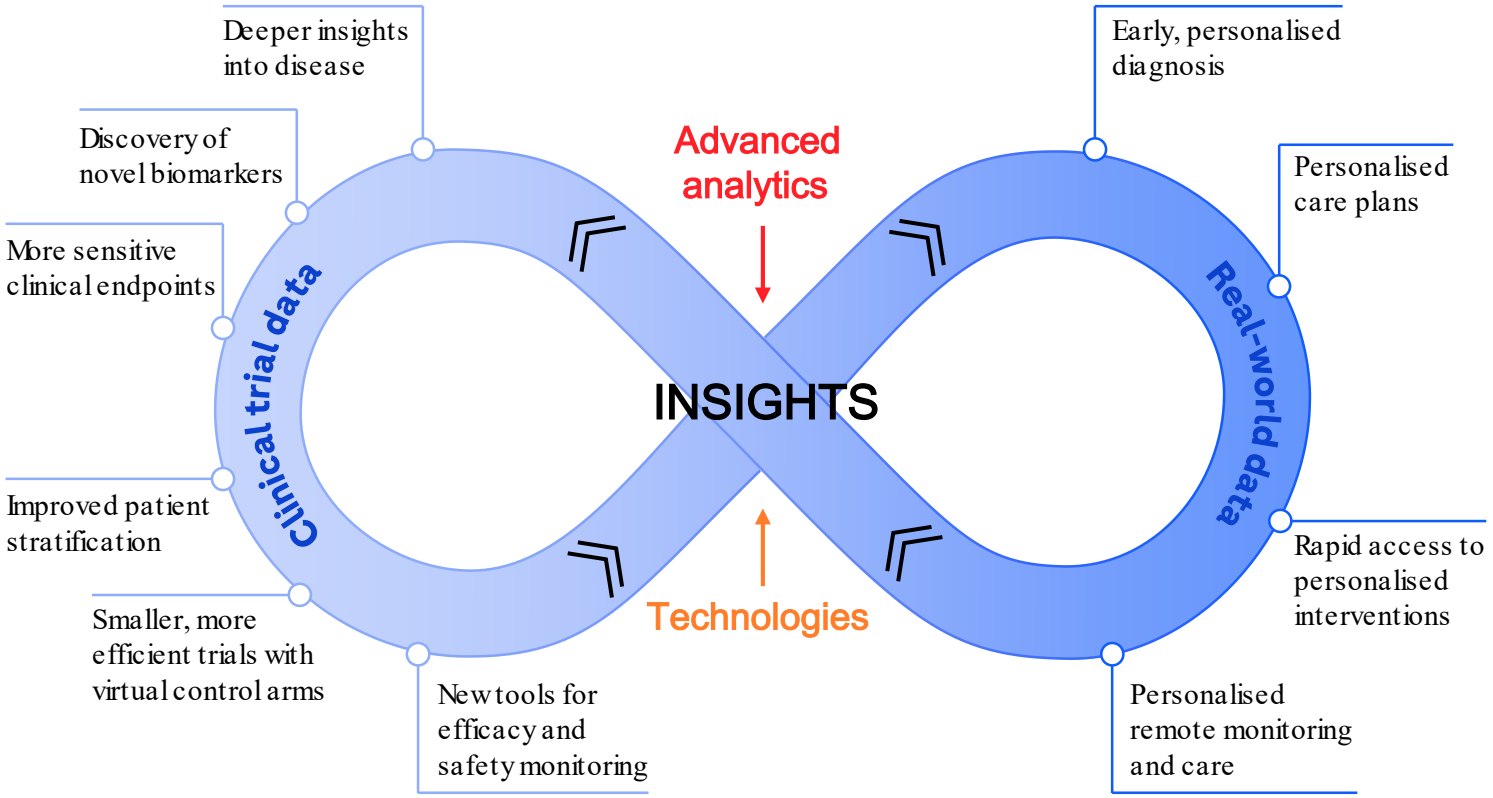
The vision of personalised healthcare



Data, **technology** and **analytics** can provide deeper insights into disease to **accelerate research and development** and **improve patient outcomes**

Adapted from Thomas, M., et al *Nature Sponsor Feature*: Aiming for higher ambition: the Roche approach to cracking the code of cancer. Available at: https://www.nature.com/articles/d42473-020-00399-z (Accessed July 2022).

A personalised approach requires integration of clinically valuable tools and involvement of varied stakeholders [1]

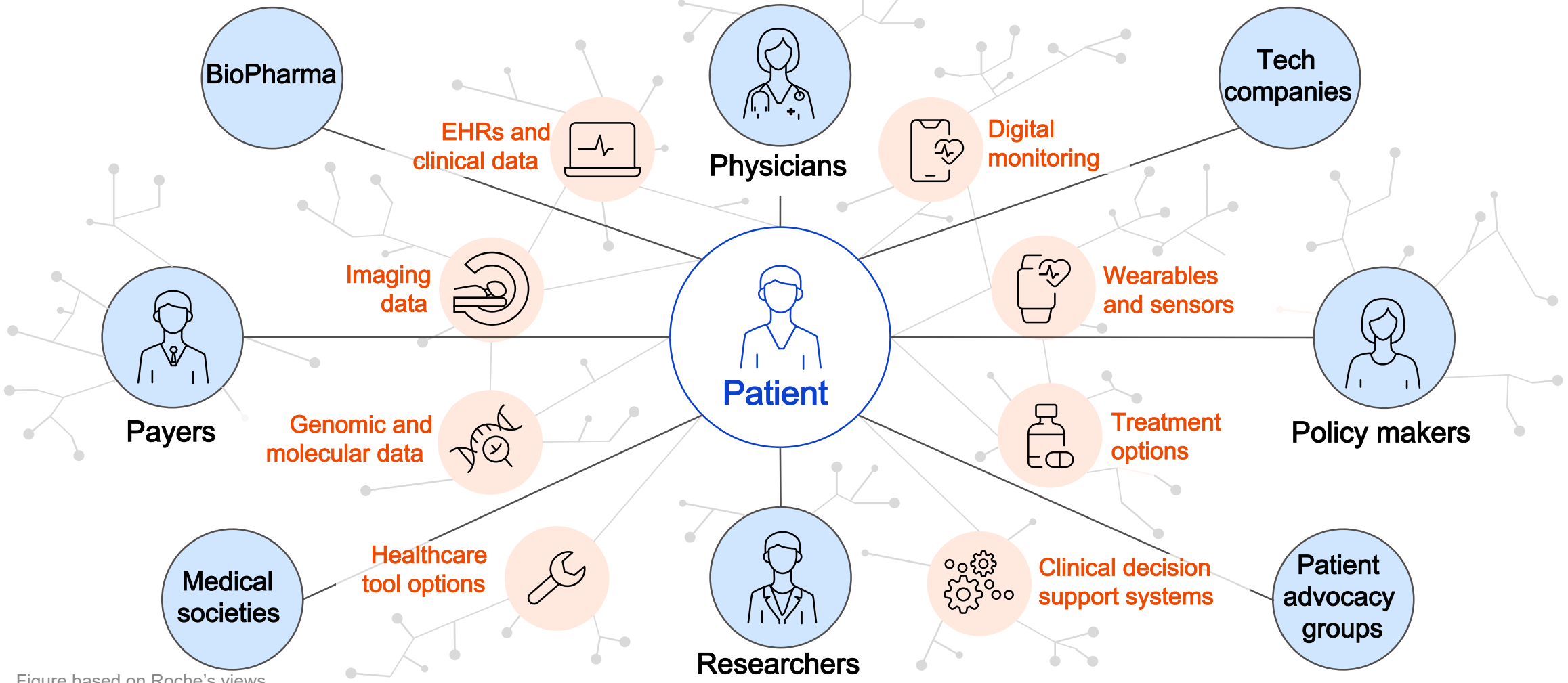
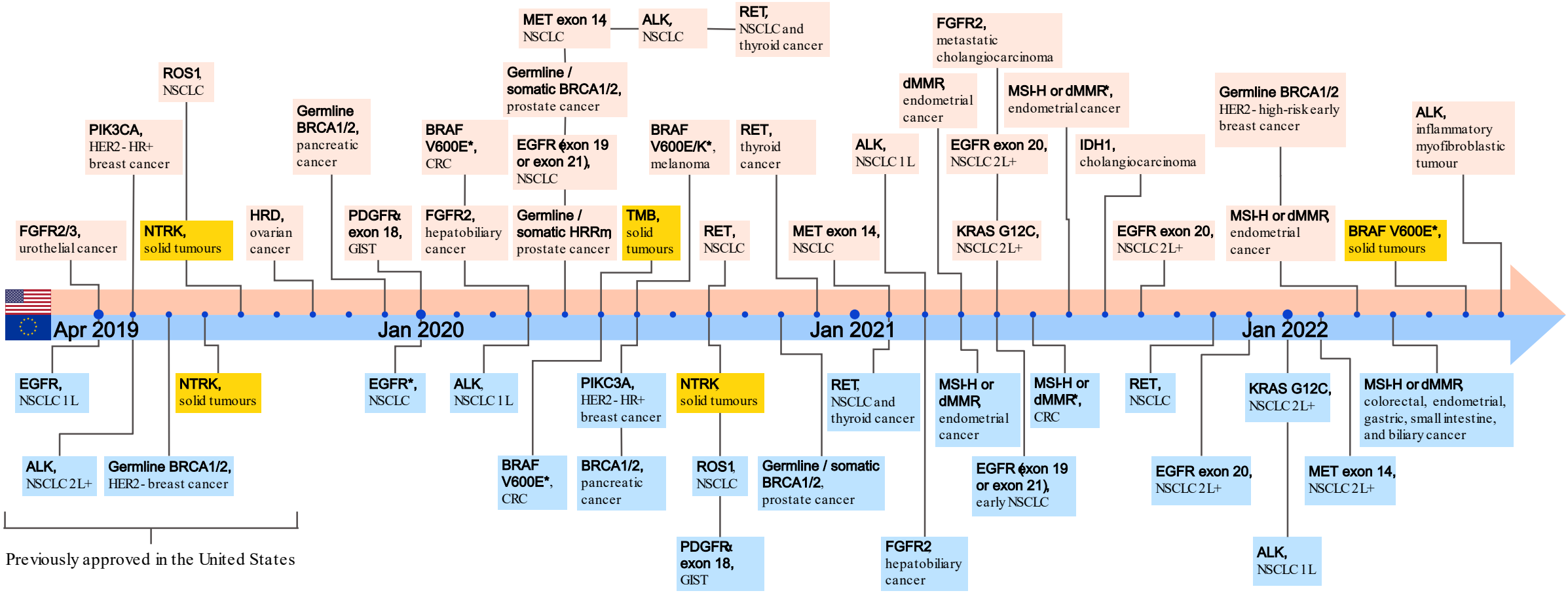


Figure based on Roche's views.

EHR: electronic health record. 1. Thomas, M, et al. *Nature Sponsor Feature*. Aiming for higher ambition: the Roche approach to cracking the code of cancer. Available at: https://www.nature.com/articles/d42473-020-00399-z (Accessed July 2022).

The number of genomic biomarker-driven drug approvals has increased in recent years

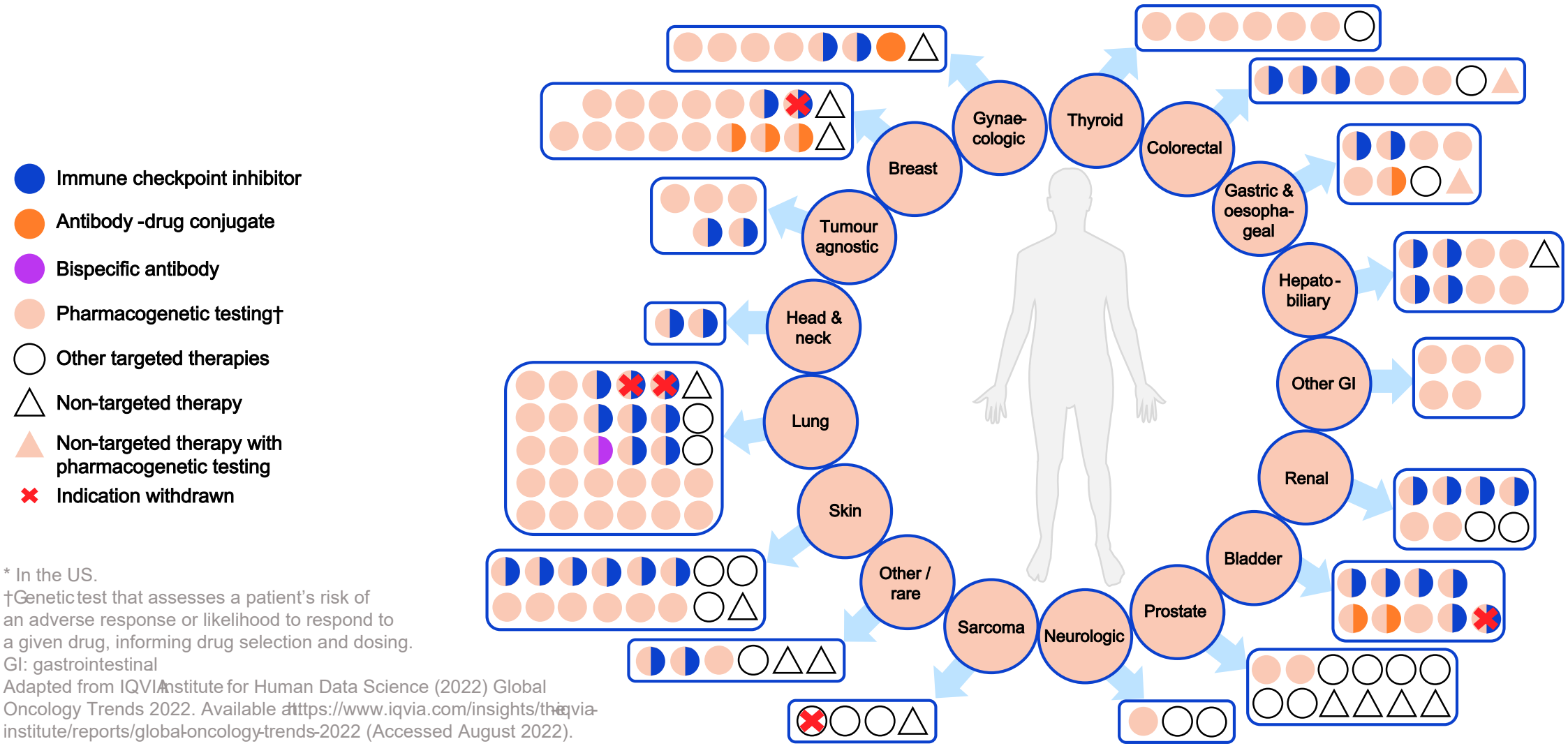


* Therapies approved as combination therapy.

CRC: colorectal cancer; dMMR: deficient mismatch repair; GIST: gastrointestinal stromal tumour; HRRm: homologous recombination repair mutation; (m)NSCLC: (metastatic) non-small cell lung cancer; MSI-H: microsatellite instability high; TMB: tumour mutational burden.

Adapted from Mateo, J., et al. (2022) *Nat Med* 28:658-65. Therapy approvals between April 2021 and July 2022 were added based on FDA/EMA genomic biomarker-dependent approvals or indication expansions. All data for this time period were obtained from the respective FDA and EMA websites.

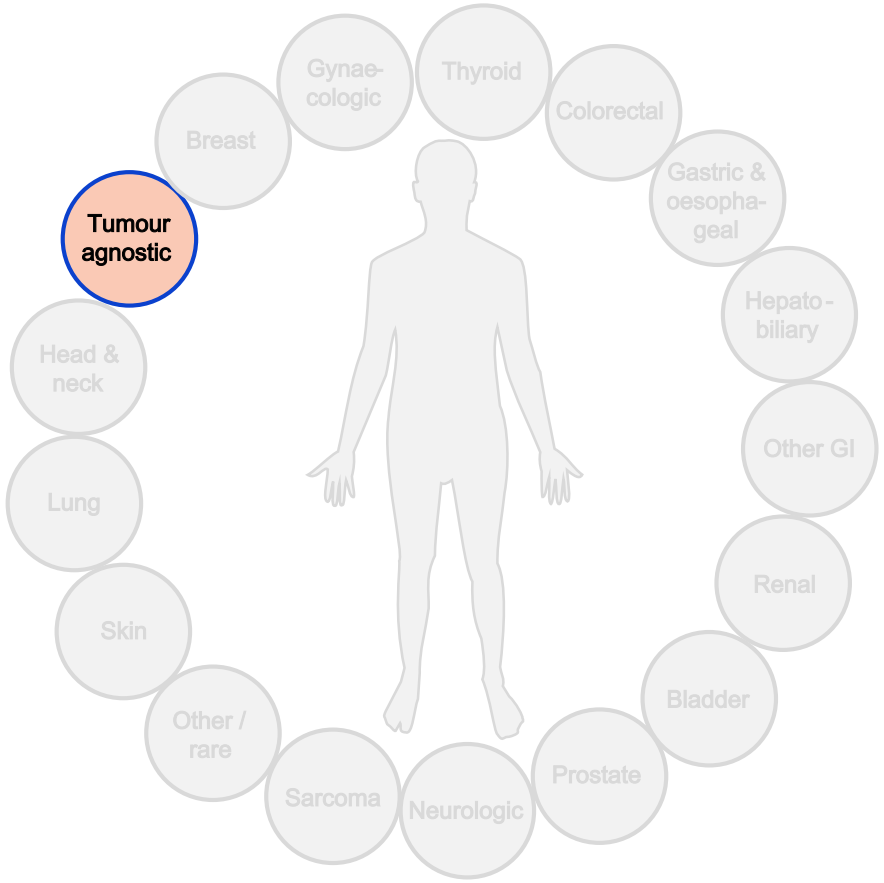
Since 2011, there have been 96 new medications in oncology, with 25 approved in multiple indications*



* In the US.
†Genetic test that assesses a patient's risk of an adverse response or likelihood to respond to a given drug, informing drug selection and dosing.
GI: gastrointestinal
Adapted from IQVIA Institute for Human Data Science (2022) Global Oncology Trends 2022. Available at https://www.iqvia.com/insights/the-iqvia-institute/reports/global-oncology-trends-2022 (Accessed August 2022).

The number of tumour agnostic biomarkers with approved treatments is projected to increase[1]

Current tumour agnostic biomarkers with FDA-approved therapies include ***NTRK*** (2), **MSI-H/dMMR**, **TMB-H**, and ***BRAF*** **V600E**



dMMR: deficient mismatch repair; FDA: Food and Drug Administration; GI: gastrointestinal; MSI-H: microsatellite instability-high; TMB-H: tumour mutational burden-high.
Adapted from IQVIA Institute for Human Data Science (2022) Global Oncology Trends 2022.

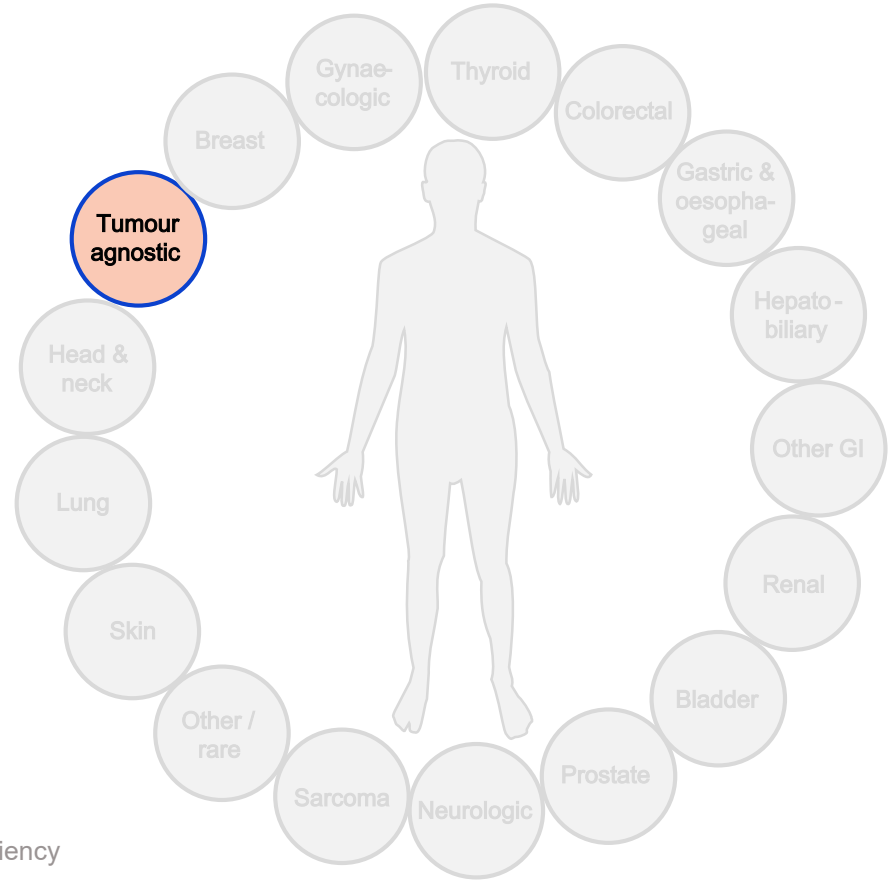
1. Thomas, M., et al. *Nature Sponsor Feature*: Aiming for higher ambition: the Roche approach to cracking the code of cancer. Available at: https://www.nature.com/articles/d42473-020-00399-z (Accessed July 2022).

The number of tumour agnostic biomarkers with approved treatments is projected to increase[1]

Over the next two years , the number of tumour agnostic biomarkers with FDA-approved therapies is **projected to increase to 15**

FGFR HRD *ATM* *BRCA* *ALK* *ROS1*

HER2 *HER4* *NRG1* *RET* *EZH2*

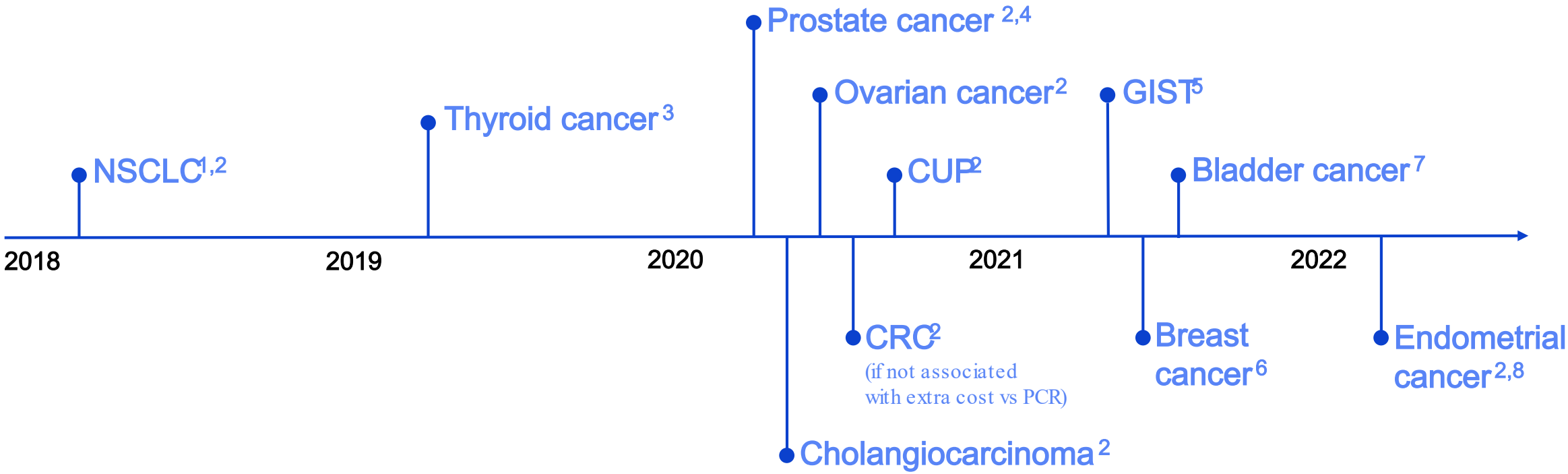


FDA: US Food and Drug Administration; GI: gastrointestinal; HRD: homologous repair deficiency
Adapted from IQVIA Institute for Human Data Science (2022) Global Oncology Trends 2022.

1. Thomas, M., et al *Nature Sponsor Feature* Aiming for higher ambition: the Roche approach to cracking the code of cancer. Available at: https://www.nature.com/articles/d42473-020-00399-z (Accessed July 2022).

ESMO recommends use of genomic testing in an increasing number of metastatic cancers

Recommendations for the **use of genomic testing** in an **ESMO guideline***



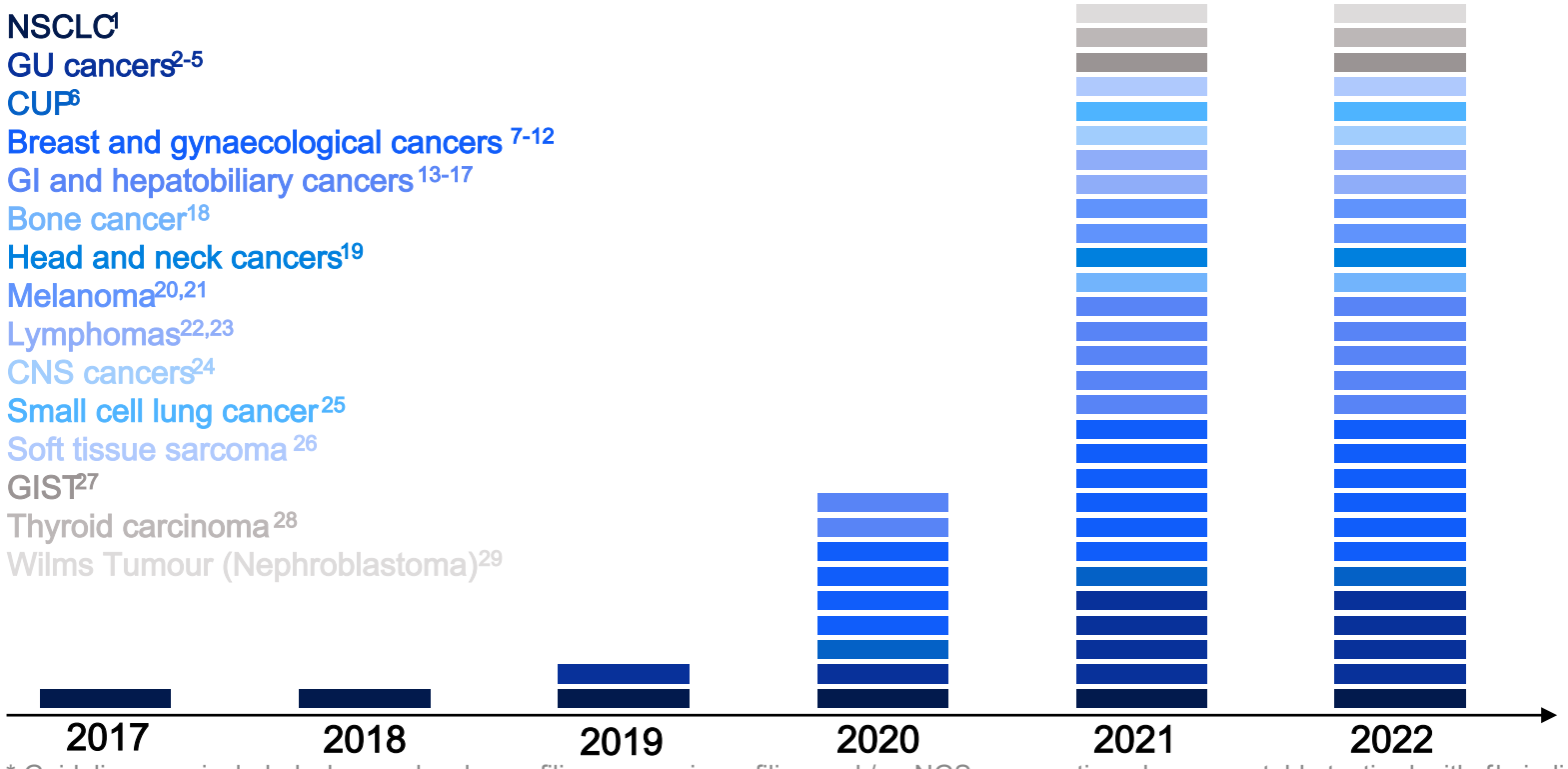
* Guidelines are included when molecular profiling, genomic profiling and / or NGS are mentioned as acceptable testing methods for individual genes or sets of genes / biomarkers in a specific guideline update. If previous versions of guidelines were not available for reference, the closest available at time of access was used as the best estimate for the timepoint of new recommendation.

CRC: colorectal cancer; CUP: cancer of unknown primary; GIST: gastrointestinal stromal tumour; NGS: next generation sequencing; mNSCLC: metastatic non-small cell lung cancer.

1. Planchard, D., et al. (2018) *Ann Oncol* 29 (suppl 4) iv192-237; 2. Mosele, F., et al. (2020) *Ann Oncol* 31:1491-1505; 3. Filetti, S., et al. (2019) *Ann Oncol* 30:1856–83;
4. Parker, C., et al. (2020) *Ann Oncol* 31:1119-34; 5. Casali, P.G., et al. (2021) *Ann Oncol* 33:20-33; 6. Gennari, A., et al. (2021) *Ann Oncol* 32:1475-95;
7. Powles, T., et al. (2021) *Ann Oncol* 33:244-58; 8. Oaknin, A., et al. (2022) *Ann Oncol* doi.org/10.1016/j.annonc.2022.05.009 (In press).

US guidelines show rapid uptake of genomic testing in various indications

Each box represents a recommendation for the **use of genomic testing** in an **NCCN guideline***



ASCO recommends patients with advanced or metastatic cancer should undergo **genomic sequencing using multi-gene panel based assays** if more than one biomarker-linked therapy is approved in the patient's disease[30]

* Guidelines are included when molecular profiling, genomic profiling and / or NGS are mentioned as acceptable testing options for individual genes or sets of genes / biomarkers in a specific guideline update. Graphical representation is based on information available at https://www.nccn.org/guidelines/category_1 (accessed December 2021 and May 2022). If previous versions of guidelines were not available for reference, the closest version available at time of access was used as the best estimate for the timepoint of new recommendation.

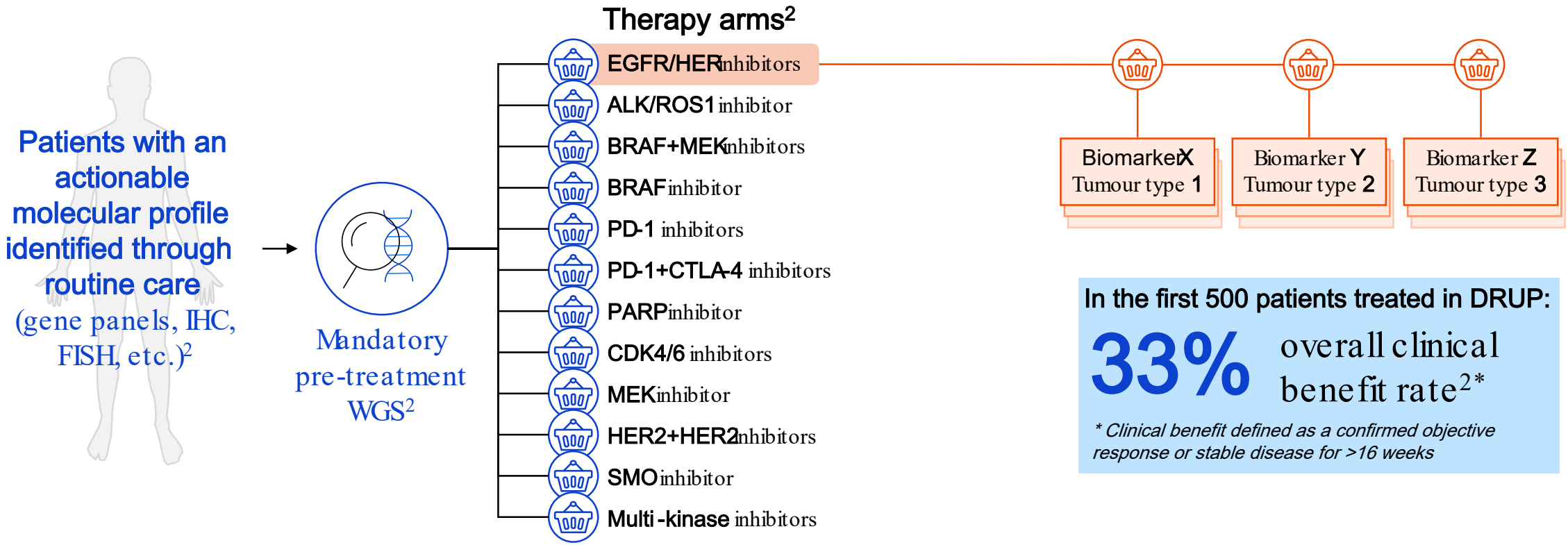
CNS: central nervous system; CUP: cancer of unknown primary; GI: gastrointestinal; GIST: gastrointestinal stromal tumour; GU: genitourinary; NGS: next-generation sequencing; NSCLC: non-small cell lung cancer.

For a full list of references, please refer to the slide notes. Please note that if a cancer type is listed for multiple years, the reference reflects the most recent version available at time of access.

The Drug Rediscovery Protocol (DRUP): An adaptive precision oncology trial

Aim

Identify signals of **efficacy** for **approved targeted therapies or immunotherapies** used **outside their label** in rare, molecularly defined subsets of patients with treatment-refractory advanced or metastatic cancer[1,2]



In the first 500 patients treated in DRUP:

33% overall clinical benefit rate[2*]

** Clinical benefit defined as a confirmed objective response or stable disease for >16 weeks*

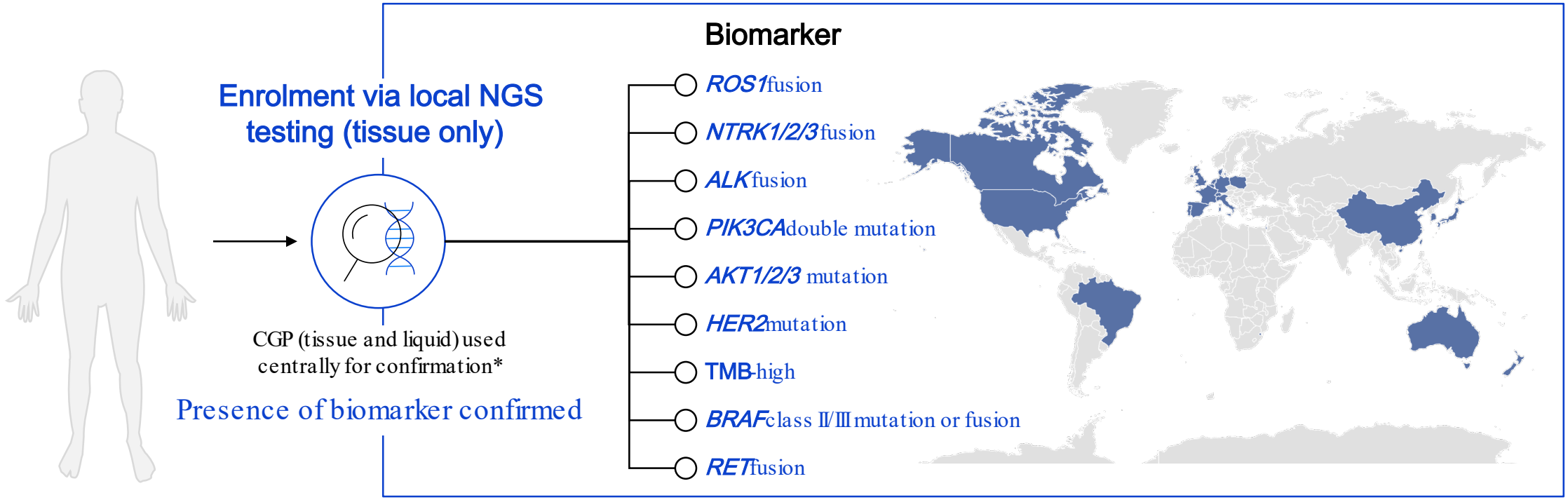
FISH: fluorescence in situ hybridisation; IHC: immunohistochemistry; WGS: whole genome sequencing.

1. van der Velden, D.L., et al. (2019) *Nature* 574:127-31; 2. Hoes, L.R., et al. (2022) *Clin Cancer Res* 28:1402-11.

TAPISTRY: An ongoing tumour-agnostic novel platform trial

Aim

Evaluate **targeted therapies or immunotherapy** in participants with unresectable, locally advanced or metastatic solid tumours harbouring **specific oncogenic genomic alterations or who are TMB-high by NGS**



* Confirmation does not impact enrolment unless patients are screened centrally by FMI.
CGP: comprehensive genomic profiling; FMI: Foundation Medicine Inc.; NGS: next-generation sequencing; TAPISTRY: Tumour Agnostic Precision Immunology and Somatic Targeting Rational for You; TMB: tumour mutational burden; WT: wild-type.

Drilon, A.E., et al. (2021) *J Clin Oncol* 39:15 supplement (ClinicalTrials.gov NCT04589845).

What's is GCP?

Comprehensive genomic profiling (CGP) is a next-generation sequencing approach, that detects novel and known variants of the four main classes of genomic alterations , and genomic signatures , to provide prognostic, diagnostic and predictive insights that inform research or treatment decisions for individual patients across all cancer types.

Comprehensive Genomic profiling (CGP) at Foundation

Medicine starts with the assessment of genomic alterations

FoundationOne comprehensively analyses* the tumour genome to identify all clinically relevant genomic alterations in a broad range of cancers. [1-4] In a single test, FoundationOne analyses >300 cancer-related genes and also reports TMB and MSI[3]

Base substitutions	Insertions and deletions	Copy number alterations	Rearrangements	TMB & MSI
✓	✓	✓	✓	✓
BRAF V600E	EGFR Exon 19 deletion	HER2 amplification	ALK Fusion	

Provides additional relevant genomic **clues** as to which patients may benefit from certain immunotherapies

*Using the Illumina® HiSeq 2000 platform, hybrid capture-selected libraries are sequenced to high uniform depth (targeting >500X median coverage with >99% of exons at coverage >100X). CGP: comprehensive genomic profiling;
MSI: microsatellite instability; TMB: tumour mutational burden.

1. Suh JH, et al. (2016) *Oncologist* 21:684-91; 2. Frampton, GM, et al. (2013) *Nat Biotechnol* 31:1023-31;
3. FoundationOne® Technical Specifications (2017)
Available at: www.foundationmedicine.com/genomic-testing/foundation-one (Accessed June 2018);
4. Schwaederle, M, et al. (2015) *Mol Cancer Ther* 14:1488-94.

FMI Reimbursement Landscape (2022 Q2)

MIDDLE EAST

Lebanon: F1cDx, all advanced cancers (exhaustion after SoC)

UAE: F1cDx & F1LcDx, all advanced cancers, Dubai only

Israel: National reimbursement of CGP for NSCLC, CRC, CUP and bladder (adult cancer patients), as well as for all pediatric cancer patients but not for send-out tests

NORTH AMERICA

USA: All products, all advanced cancers

LATAM

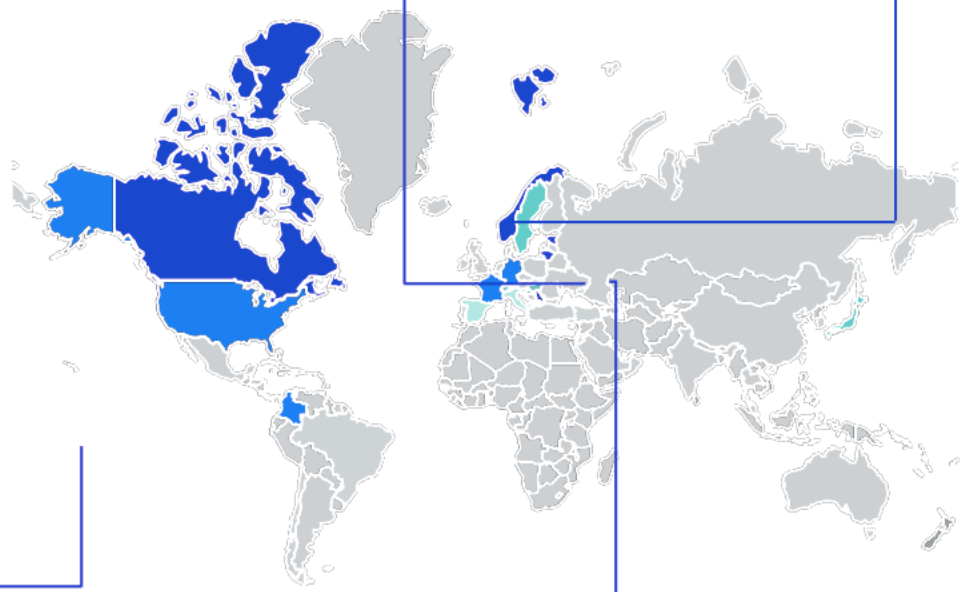
Colombia: F1cDx & F1LcDx, all advanced cancers [limited funding]

Mexico: F1cDx in NSCLC

APAC

Japan: F1cDx & F1LcDx, all advanced cancers

Korea: National reimbursement of CGP but not for send-out tests



Ongoing submissions

Taiwan, Serbia, Lithuania, Estonia, The UK, Slovakia, Bulgaria

EUROPE

Germany: F1cDx, all advanced cancers, outpatient only

Switzerland: F1cDx, F1LcDx, F1H, all advanced cancers

France: F1cDx, all advanced cancers [temporary code]

Croatia: F1cDx, all newly diagnosed metastatic cancer patients

Sweden: F1cDx, 6 cancer types (NSCLC, BC, CRC, CUP, OC, MM)

Latvia: F1cDx & F1LCDx in aNSCLC

Italy: F1cDx & F1LcDx, all advanced cancers, Emilia-Romagna and Lombardy regions

Spain: F1cDx & F1LcDx, NSCLC, CUP, rare cancers, Balnearic islands only

Austria: F1cDx & F1LcDX, all tumor types

Hungary: F1cDx in aNSCLC

Norway: F1cDx, TMB + NSCLC [limited funding]

Czech Republic*

Source: Internal data, last update 2022 Q2

**Limited funding, currently patients are allowed to 2DNA&2RNA testing per year*

Doing now what patients need next