



# Burning Rock Biotech Limited

## 1Q 2024 results

29 May 2024

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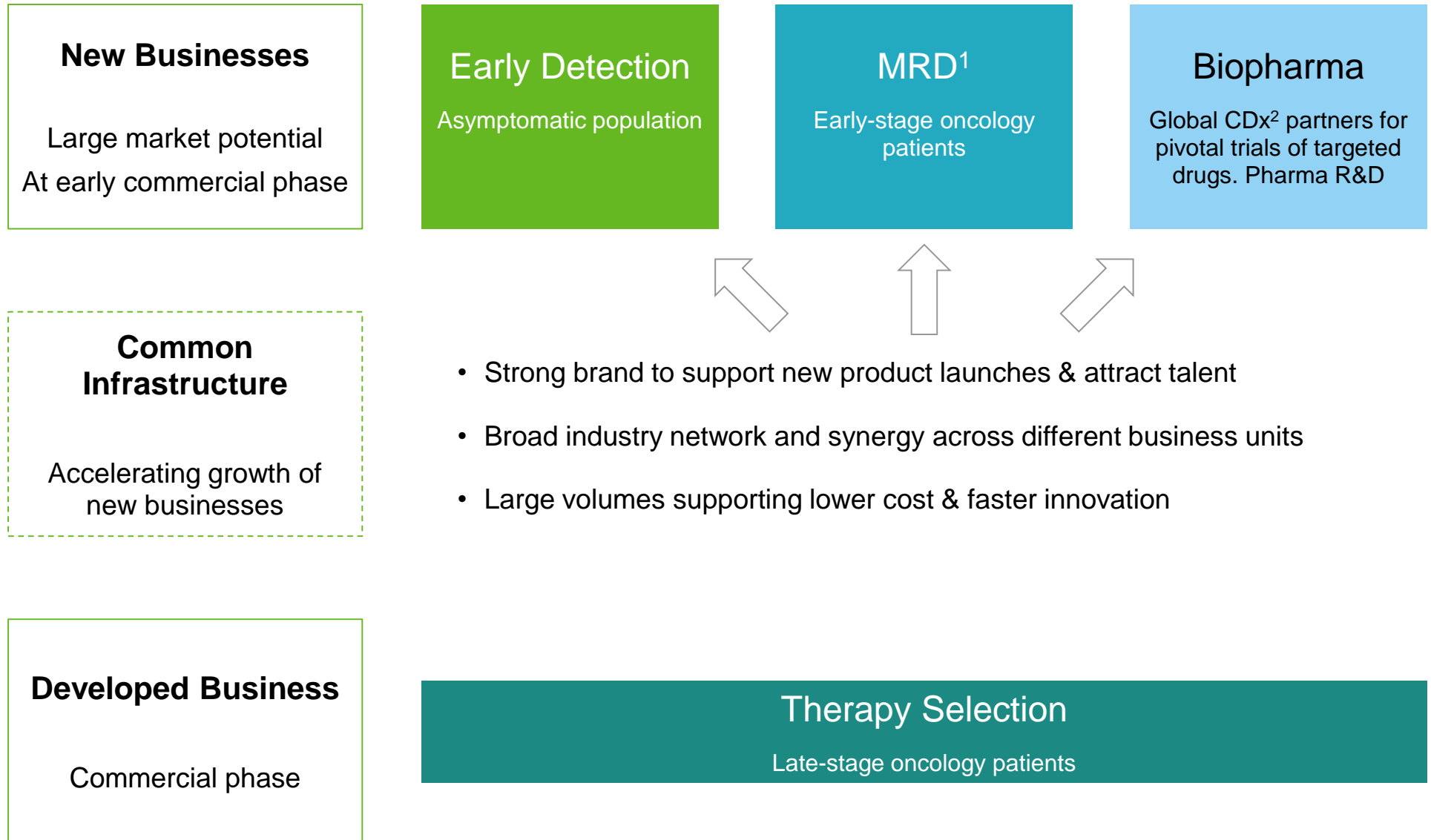
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# Our value-building blocks

Extending leadership in NGS-based precision oncology from late-stage to earlier stage patients



Notes:

<sup>1</sup> Minimal residual disease of solid tumors

<sup>2</sup> Companion diagnostics

# Recent progress

Continued efficiency gains, driving towards profitability

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## Delivering results on

### 1 Driving sales efficiency

- Increasing sales productivity per head
- Benefiting from more rational industry competition

### 2 Improving gross margin

- Leveraging our scale
- Delivering on margin improvement projects

### 3 Reducing G&A expenses

- Cutting overhead and lowering fixed cost-base

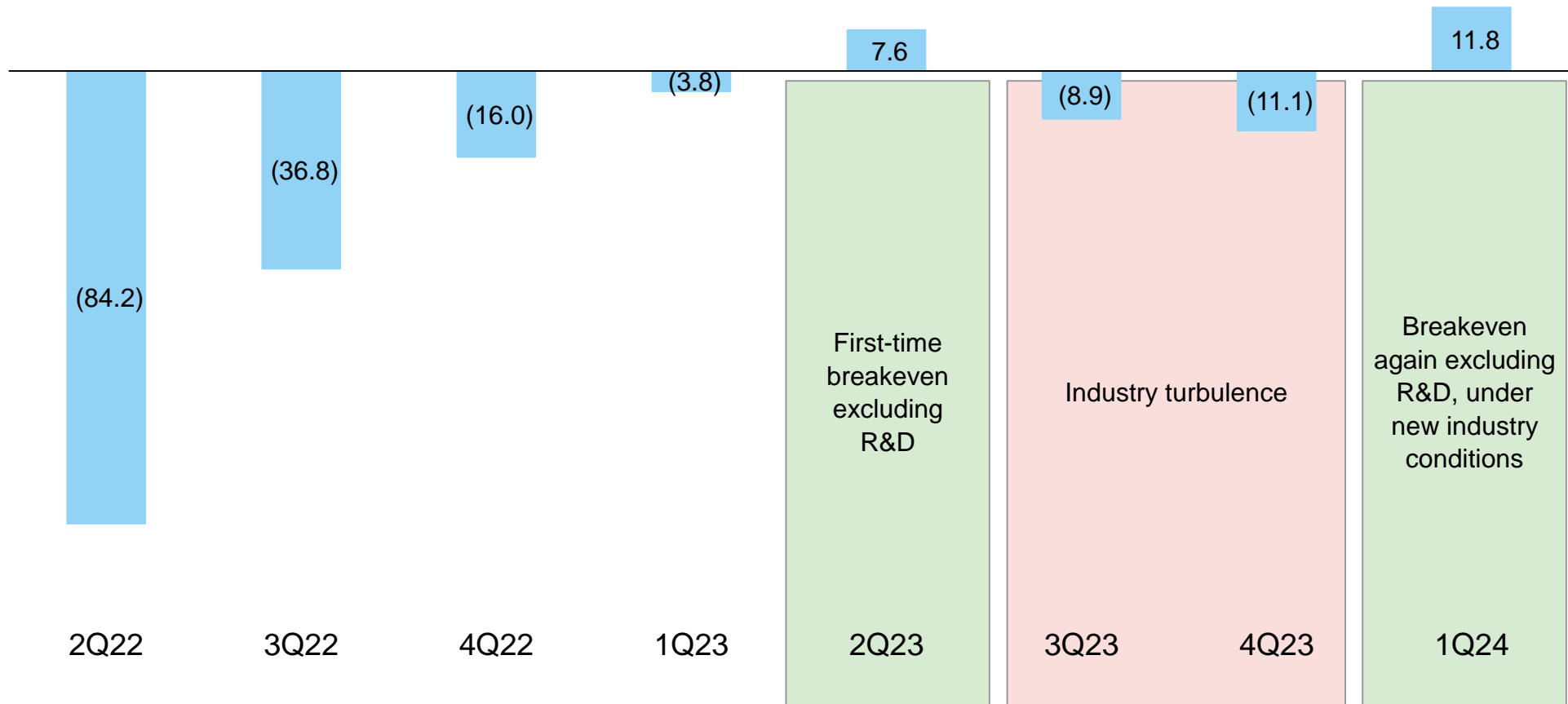
### 4 Reducing R&D expenses

- As clinical programs complete and run down
- Disciplined on new investment

# 1Q24 getting to commercial breakeven under new industry conditions

Breakeven defined as Non-GAAP gross profit *minus* SG&A\*

Non-GAAP gross profit *minus* SG&A\* (RMB millions)



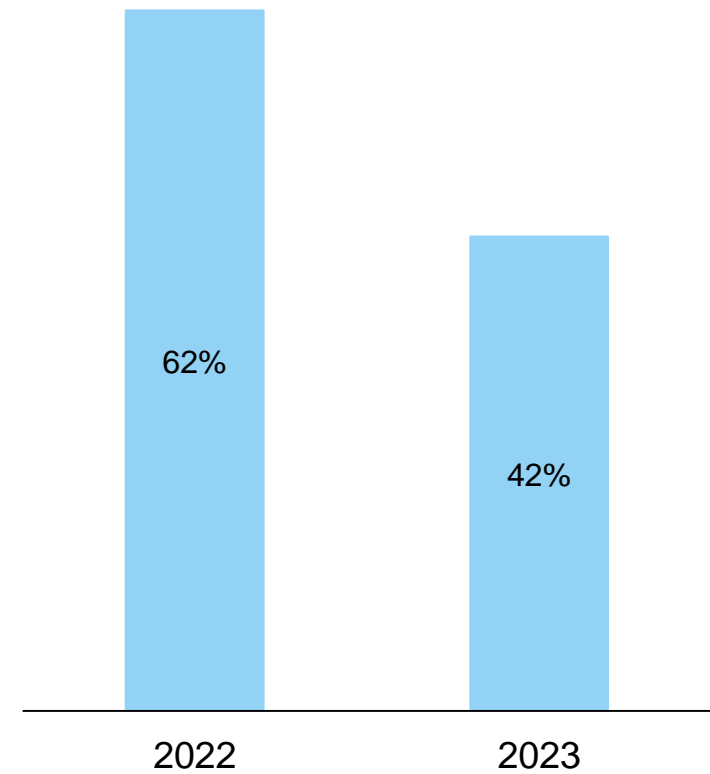
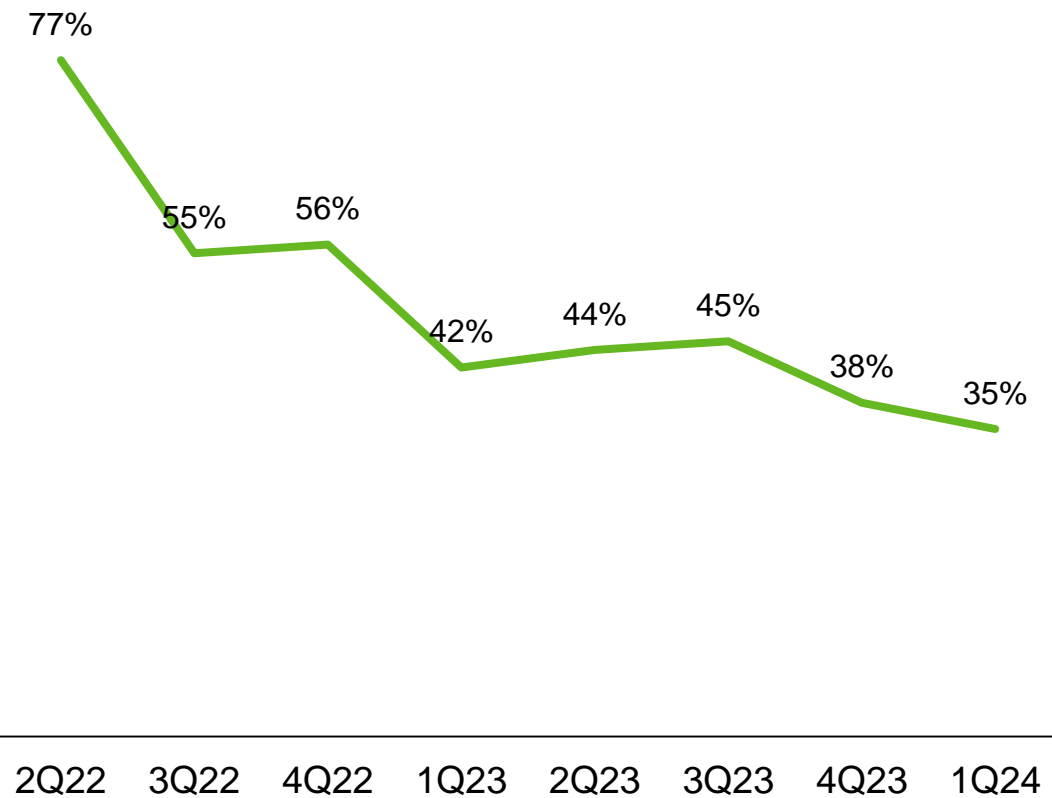
Notes:

\* Non-GAAP gross profit, which is defined as gross profit excluding depreciation and amortization. Non-GAAP SG&A refers to selling and marketing expenses and general and administrative expenses, both excluding their respective share-based compensation and depreciation and amortization.

# 1 Driving sales efficiency

Expect below 40% selling expense going forward

Non-GAAP sales and marketing expenses as % of revenue\*



Notes:

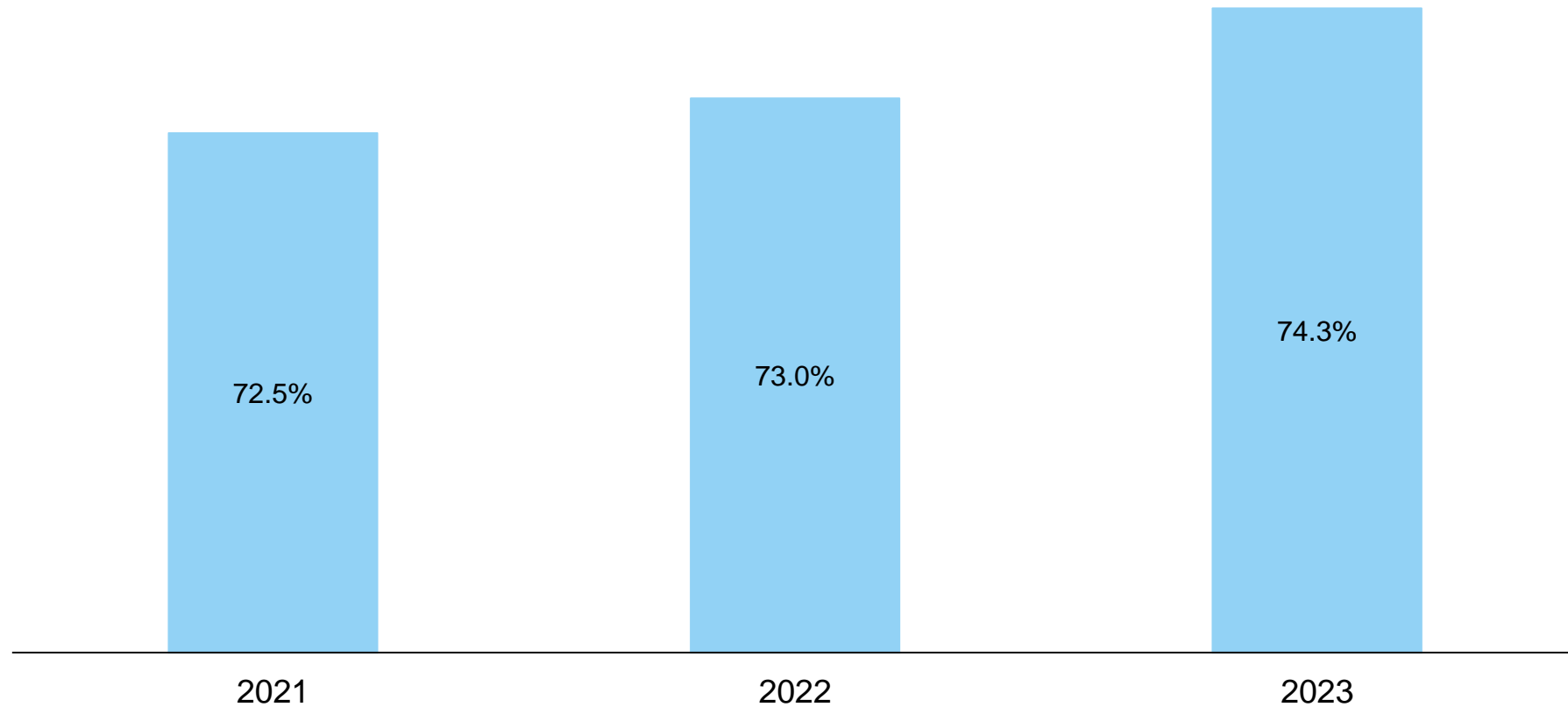
\* Excluding share based compensation (SBC) and depreciation and amortization (D&A)

## 2 Improving gross margin

### Delivering on margin improvement initiatives

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Non-GAAP gross profit as % of revenue\*



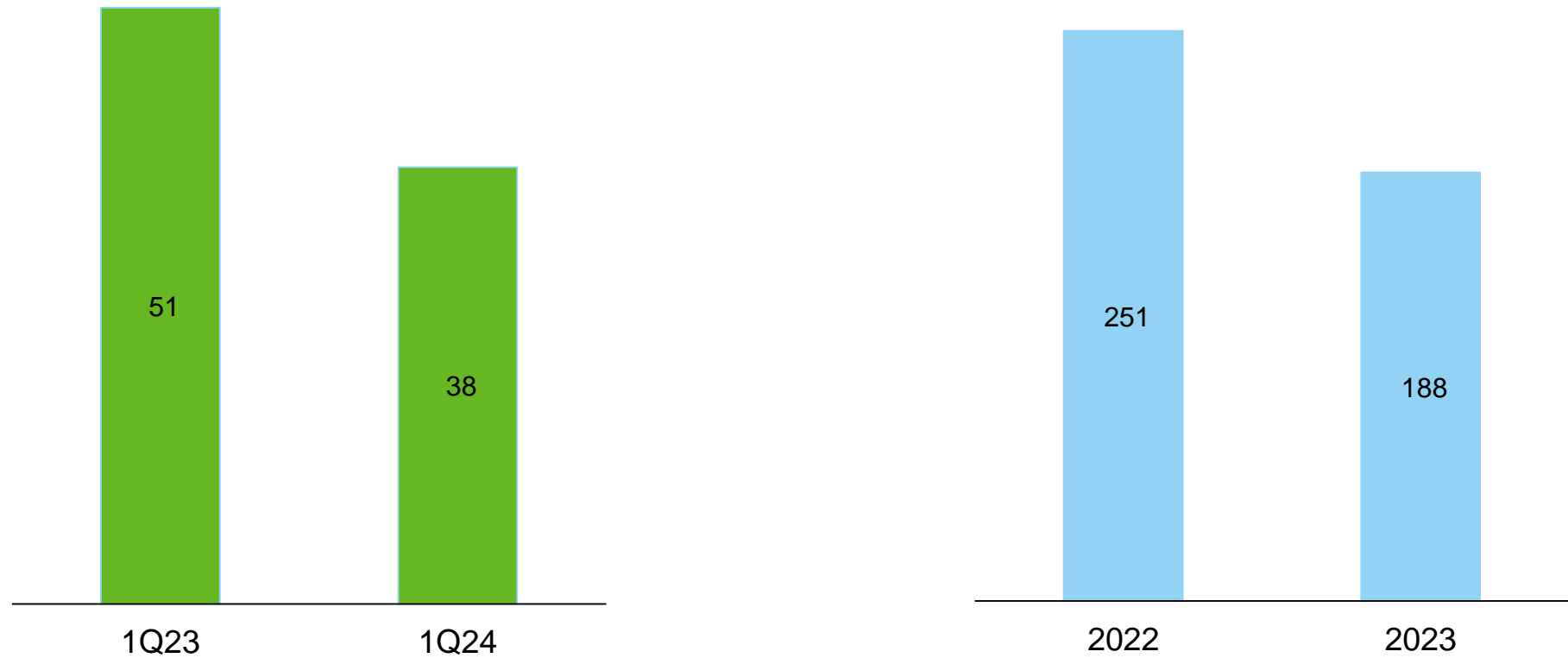
Notes:

\* Non-GAAP gross margin, which is defined as gross margin excluding depreciation and amortization (D&A)

### 3 Reducing G&A expenses

Expect additional cost savings going into 2024

Non-GAAP general and admin expenses\* (RMB millions)



Notes:

\* Excluding share based compensation (SBC) and depreciation and amortization (D&A)



# Strong cash position to fund operations for the next 3 years

Commercial operation (excluding R&D expenses) reached profitability in 1Q24

On R&D spend, disciplined investment in R&D

RMBm	2022	2023	1Q2024	2024E <sup>1</sup>
Operating cash outflow <sup>2</sup>	457	256	40	
Capex <sup>3</sup>	75	9	3	
Sum	532	265	43	c.150-200
Cash balance at period-end <sup>4</sup>	925	615	573	

Notes:

<sup>1</sup> Based on management's current estimate and subject to change

<sup>2</sup> Net cash used in operating activities

<sup>3</sup> Purchase and prepayment of property and equipment and intangible assets, issuance of convertible loan, out of investing cashflows

<sup>4</sup> Consists of Cash and cash equivalents of approximately RMB573m and restricted cash of approximately RMB0.06m as of the end of 1Q2024

# Financials

Steady progress of improving margins, profitability and reducing cash outflows

RMB millions	2022	2023	YoY	1Q23	2Q23	3Q23	4Q23	1Q24	1Q24 YoY	1Q24 QoQ
<b>Revenues</b>	<b>563.1</b>	<b>537.3</b>	<b>-5%</b>	<b>142.6</b>	<b>146.2</b>	<b>127.6</b>	<b>121.0</b>	<b>125.6</b>	<b>-12%</b>	<b>4%</b>
Central lab	314.8	232.8	-26%	61.8	66.2	53.5	51.3	47.6	-23%	-7%
In-hospital <sup>1</sup>	175.3	188.6	8%	51.6	53.8	54.5	28.7	57.4	11%	100%
Pharma	73.0	115.9	59%	29.2	26.2	19.6	41.0	20.6	-29%	-50%
<b>Non-GAAP gross profit<sup>2</sup></b>	<b>411.0</b>	<b>399.4</b>	<b>-3%</b>	<b>107.9</b>	<b>109.4</b>	<b>95.1</b>	<b>87.1</b>	<b>93.0</b>	<b>-14%</b>	<b>7%</b>
<b>Total opex</b>	<b>1,360.5</b>	<b>1,032.4</b>	<b>-24%</b>	<b>287.2</b>	<b>236.1</b>	<b>264.7</b>	<b>244.4</b>	<b>211.6</b>	<b>-26%</b>	<b>-13%</b>
R&D <sup>3</sup>	344.4	264.8	-23%	74.0	73.1	64.2	53.5	49.0	-34%	-8%
S&M <sup>3</sup>	350.6	227.4	-35%	60.5	64.7	56.8	45.4	43.7	-28%	-4%
G&A <sup>3</sup>	250.5	188.3	-25%	51.2	37.1	47.2	52.8	37.5	-27%	-29%
SBC	325.1	258.4		77.8	37.2	72.7	70.7	68.8		
D&A	89.9	93.5		23.7	24.0	23.8	22.0	12.6		
<b>Non-GAAP GP – SG&amp;A</b>	<b>(190.1)</b>	<b>(16.3)</b>		<b>(3.8)</b>	<b>7.6</b>	<b>(8.9)</b>	<b>(11.1)</b>	<b>11.8</b>		
<b>Operating profit</b>	<b>(980.3)</b>	<b>(669.3)</b>		<b>(188.5)</b>	<b>(135.7)</b>	<b>(178.8)</b>	<b>(166.3)</b>	<b>(125.8)</b>		
<b>Net operating cash flows</b>	<b>(456.9)</b>	<b>(255.7)</b>		<b>(113.1)</b>	<b>(79.2)</b>	<b>(47.4)</b>	<b>(16.0)</b>	<b>(40.2)</b>		
<b>Margins</b>										
Non-GAAP GP margin <sup>2</sup>	73.0%	74.3%		75.7%	74.8%	74.5%	72.0%	74.0%		
Opex <sup>3</sup> / revenue	168%	127%		130%	120%	132%	125%	104%		
S&M <sup>3</sup> / revenue	62%	42%		42%	44%	45%	38%	35%		

Notes:

<sup>1</sup> Within in-hospital segment, over 95% revenues are kit revenues, which are recurring in nature; the remaining are instrument revenues. In-hospital primarily through direct-sales model

<sup>2</sup> Non-GAAP gross profit or margin, which is defined as gross profit or margin excluding depreciation and amortization (D&A)

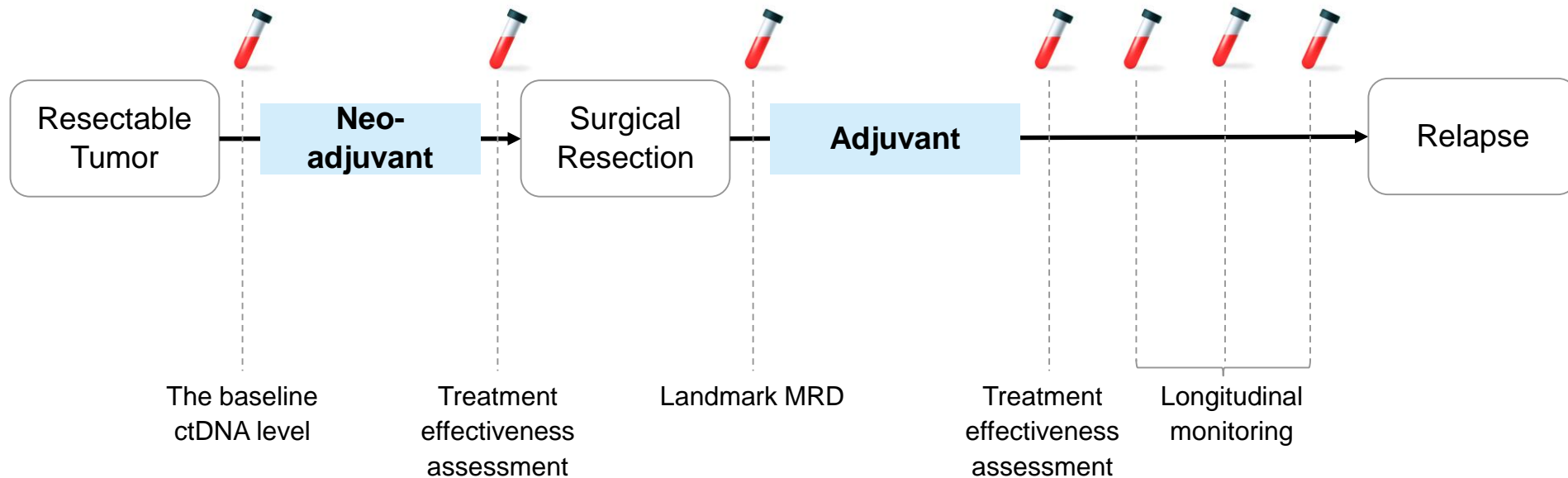
<sup>3</sup> Excluding share based compensation (SBC) and depreciation and amortization (D&A)



## Minimal Residual Disease (MRD)

# Burning Rock's MRD clinical publications

Covering adjuvant and relapse settings in lung, colorectal, gastric and other cancers



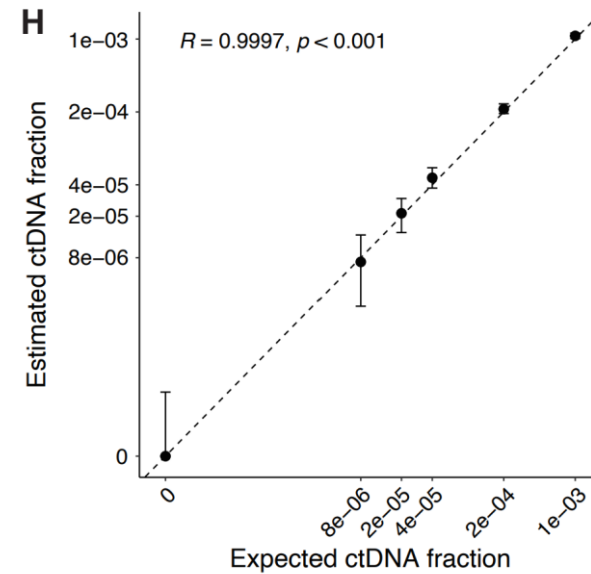
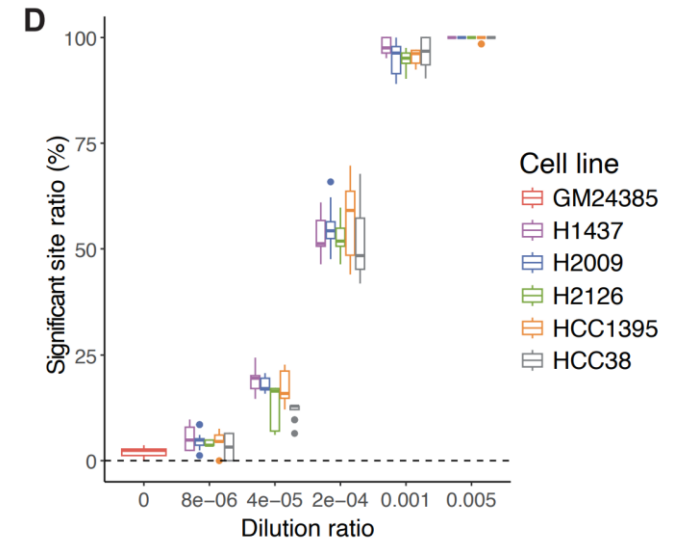
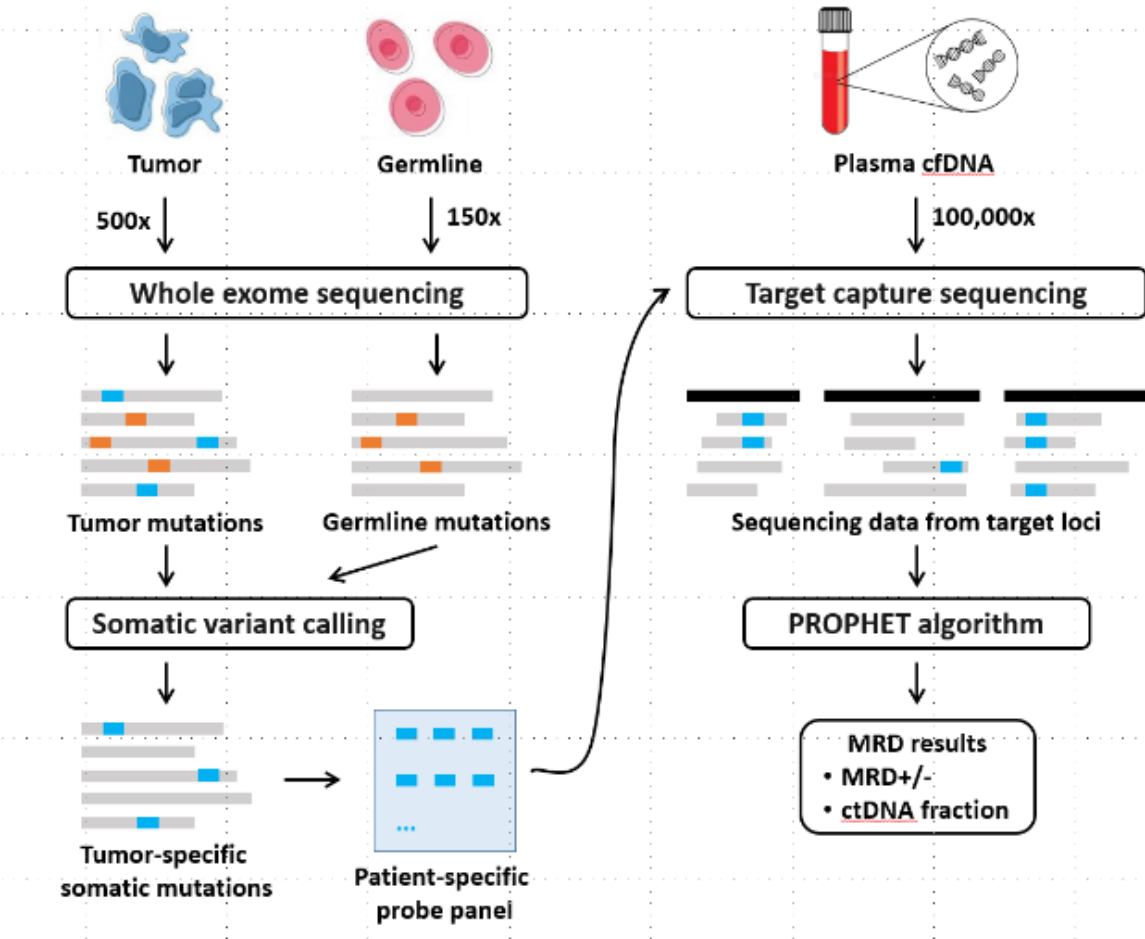
Non-small-cell lung cancer	Baseline, landmark and longitudinal monitoring timepoints completed AACR 2022 Abstract 5916, AACR 2023 Abstract 1039, MEDAL study publication
Colorectal cancer	Baseline and landmark timepoints AACR 2022 Abstract 5917, ASCO GI 2023 Abstract 213
Gastric cancer	Baseline and landmark timepoints AACR 2023 Abstract 6682
Pancreatic cancer	Baseline, landmark and longitudinal monitoring timepoints completed ASCO GI 2023 Abstract 744
Biliary tract cancer	Baseline and landmark timepoints AACR 2023 Abstract 6682

Cancer Cell

# Overview of brPROPHET™

## An ultrasensitive and quantitative MRD assay

### Overview of the PROPHET assay



# MEDAL study

## Personalized MRD using brPROPHET™ on non-small cell lung cancer (NSCLC)

### Cancer Cell

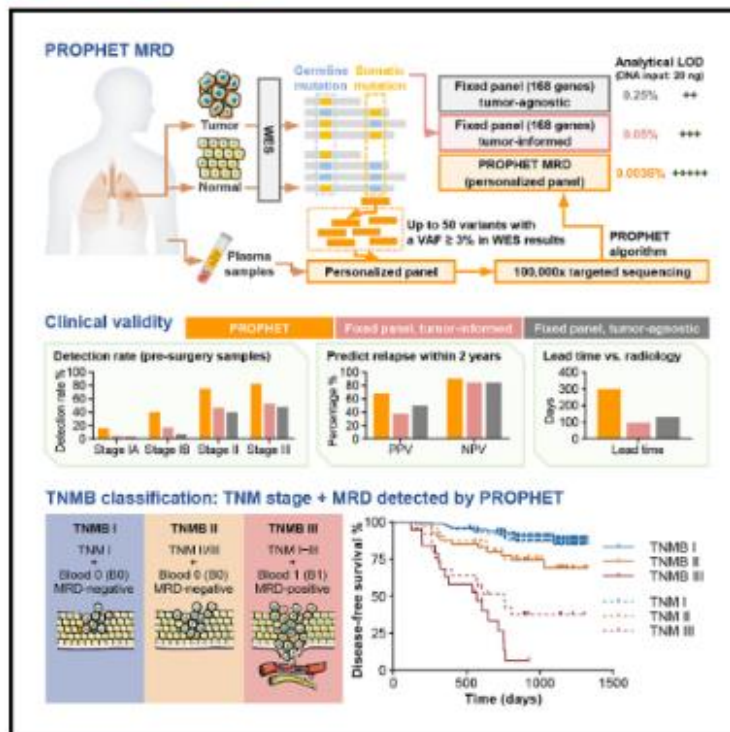
Article

#### Highlights

- PROPHET outperforms fixed-panel MRD assays in head-to-head comparison in NSCLC
- TNMB stage, integrating landmark ctDNA MRD and TNM, improves prognosis prediction
- PROPHET illustrates a median lead time of 299 days to radiological recurrence
- Post-relapse ctDNA status facilitates decision on later lines of treatment

## Individualized tumor-informed circulating tumor DNA analysis for postoperative monitoring of non-small cell lung cancer

#### Graphical abstract



#### Authors

Kezhong Chen, Fan Yang, Haifeng Shen, ..., David Carbone, Zhihong Zhang, Jun Wang

#### Correspondence

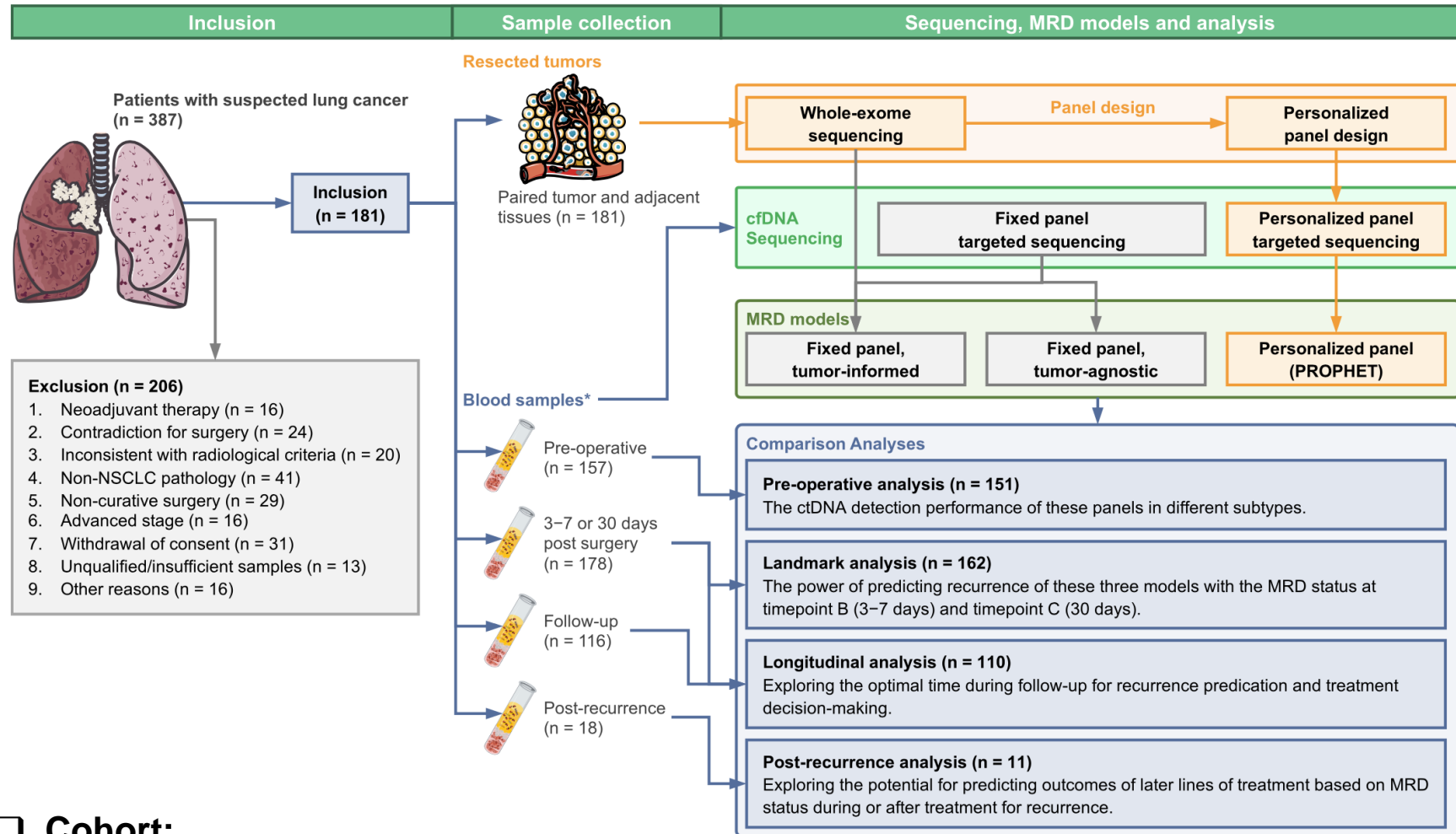
chenkezhong@pkuph.edu.cn (K.C.), zhihong.zhang@brbiotech.com (Z.Z.), wangjun@pkuph.edu.cn (J.W.)

#### In brief

Chen et al. introduced personalized Patient-specific pROgnostic and Potential tHERapeutic marker Tracking (PROPHET) for detecting molecular residual disease (MRD) in NSCLC, featuring a notably low limit of detection (LOD). It exhibits elevated sensitivity and extended lead time than radiologically confirmed recurrence. It also facilitates prognostic accuracy and postoperative treatment evaluation.

Chen et al., 2023, *Cancer Cell* 41, 1–14  
October 9, 2023 © 2023 Published by Elsevier Inc.  
<https://doi.org/10.1016/j.ccell.2023.08.010>

# Study design



## □ Cohort:

- 181 patients enrolled Stage I (63%), II (19%), and III (18%)

## □ Sampling Time:

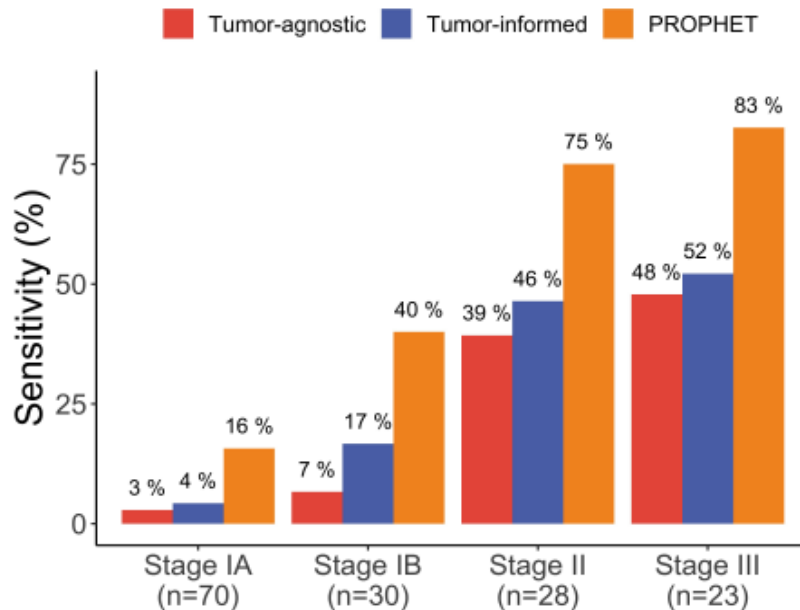
- Tumor and adjacent paired tissue collected at surgery
- Blood samples collected at Pre-operative, 3 days, and 30 days post-surgery
- Median Follow-up Time: 30 months

# brPROPHET™ demonstrates superior sensitivity in ctDNA detection

## Clinical validation with pre-operative plasma samples

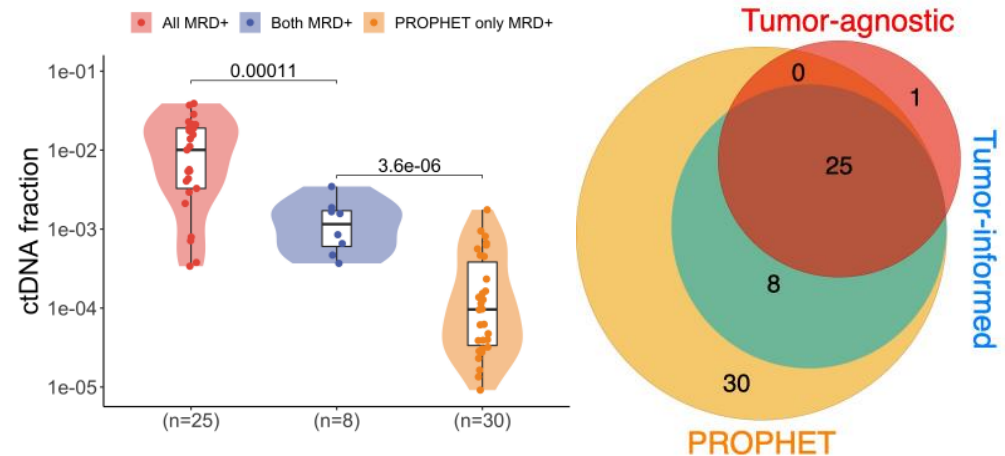
(a)

Sensitivity of pre-operative plasma



(b)

ctDNA fraction distribution of MRD (+) samples detected by different methods

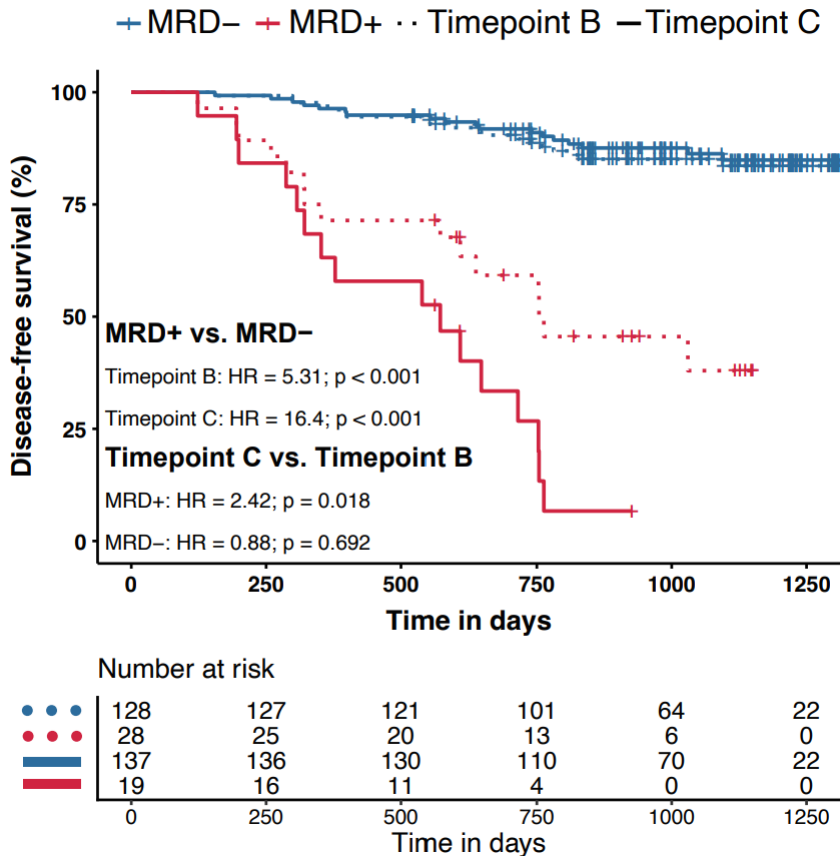


- For pre-operative plasma from patients with different clinical stages, brPROPHET has a higher sensitivity than the other two methods
- The median ctDNA fraction of the 30 patients detected by PROPHEt alone was significantly lower than the 25 patients detected by all three MRD assays

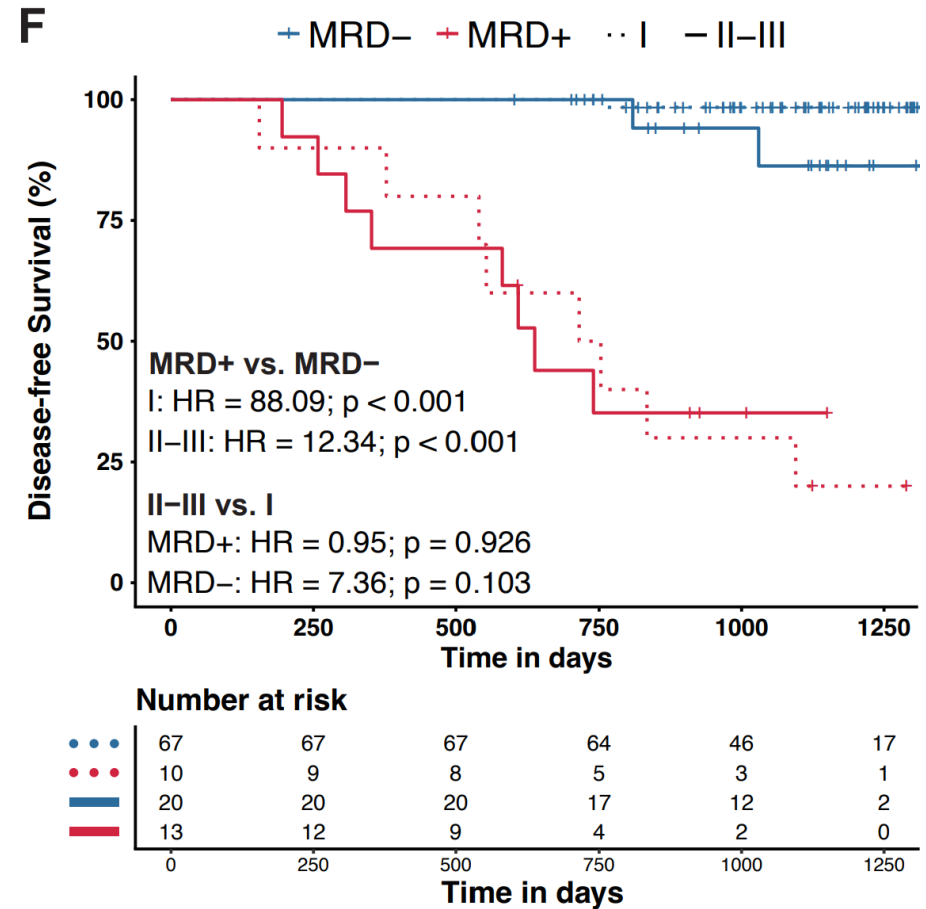
The patient-specific brPROPHET has a higher sensitivity than the two fixed panel detection methods



# brPROPHET™ shows strong prognostic value in post-surgery NSCLC patients



Prognostic analysis at **Landmark** time points



Longitudinal MRD analysis

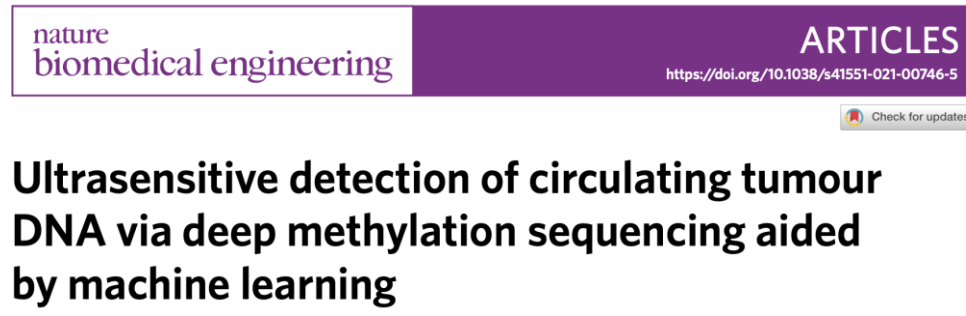


**Early detection**

# Burning Rock's multi-cancer early detection technology

## Competitive technology


Methylation + machine learning to overcome challenges of low ctDNA abundance




nature biomedical engineering ARTICLES  
https://doi.org/10.1038/s41551-021-00746-5  
Check for updates

### Ultrasensitive detection of circulating tumour DNA via deep methylation sequencing aided by machine learning

## Multi-cancer validation data



Annals of Oncology  
Available online 26 February 2023  
In Press, Journal Pre-proof ? What's this? >



Original Article

### Unintrusive multi-cancer detection by circulating cell-free DNA methylation sequencing (THUNDER): development and independent validation studies

AACR 2022

Session OPO.CL11.01 - Biomarkers  
**5116 - Analytical performance of ELSA-seq, a blood-based test for early detection of multiple cancers**

Session OPO.CL11.01 - Biomarkers  
**5109 - Development of cfDNA reference standards for methylation-sequencing tests**

ESMO 2022

**A multi-cancer early detection model based on liquid biopsy of multi-omics biomarkers: A proof of concept study (PROMISE study)**

## Regulatory breakthrough

 breakthrough device designation granted

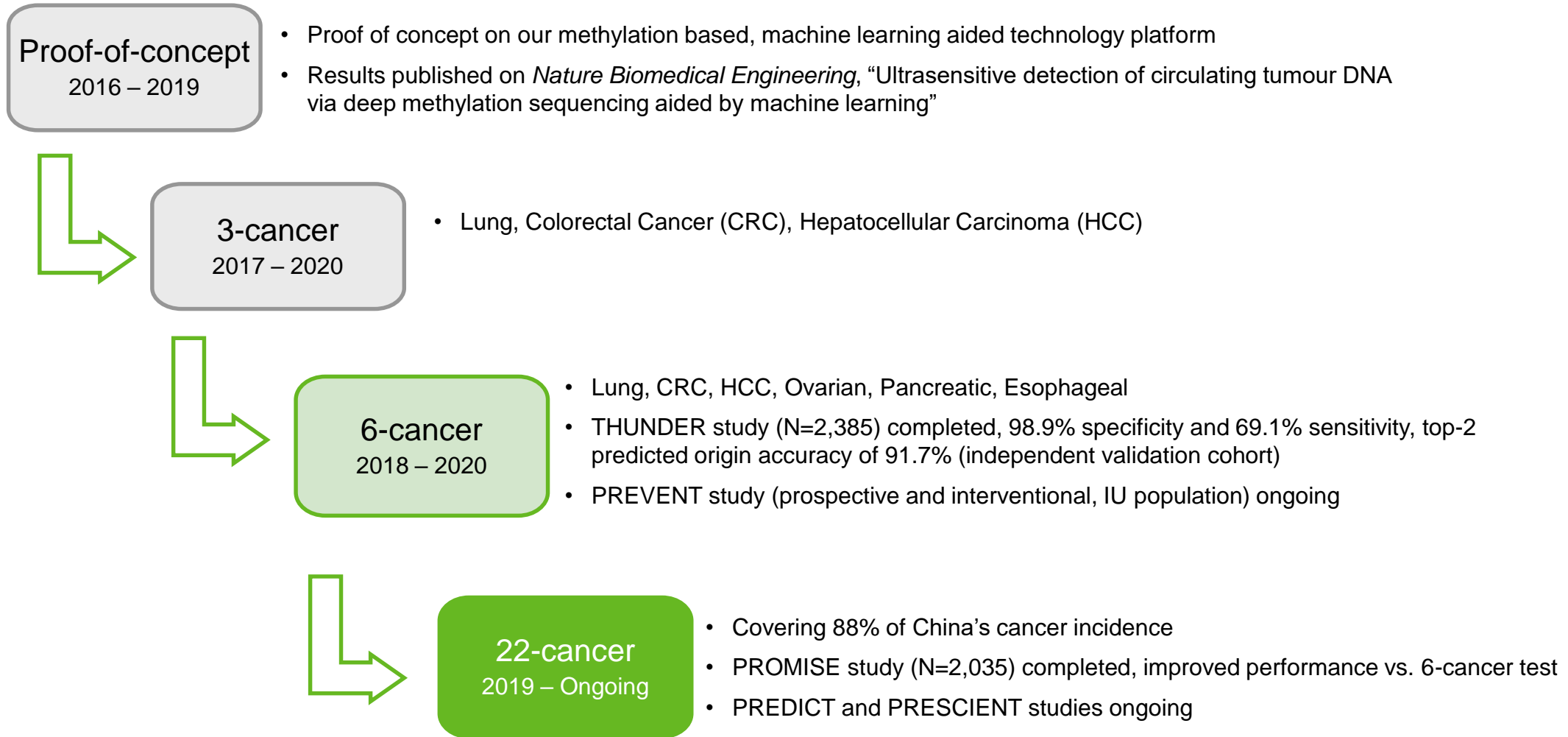


**国家药品监督管理局**  
National Medical Products Administration

China NMPA breakthrough designation granted

# Product development roadmap

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# Running the largest clinical programs in China supported by top physicians

## PREDICT



- Leading site: Shanghai Zhongshan Hospital
  - One of China's largest comprehensive academic hospitals
  - Performs c.104,000 operations and serves c.169,000 inpatients and over 4,236,000 outpatients on an annual basis<sup>1</sup>
  - Ranked top 5 in the 2019 China's general hospital rankings<sup>2</sup>

Principal Investigator: Prof. Jia Fan



- Fellow of the Chinese Academy of Sciences
- President of Shanghai Zhongshan Hospital

## PRESCIENT



- Leading site: Cancer Hospital of the Chinese Academy of Medical Sciences<sup>3</sup>
  - The first and top cancer-specialist hospital in China
  - The National Clinical Center for Cancer Research, the National Center for Quality Control on Standardized Cancer Treatment and Diagnosis, the National Clinical Center for Drug Research

Principal Investigators

Prof. Jie He



Prof. Jie Wang



- Fellow of the Chinese Academy of Sciences
- President of CHCAMS
- Head of the Dept. of Medicine, CHCAMS

## PREVENT



四川大学华西医学中心  
WEST CHINA MEDICAL CENTER OF SICHUAN UNIVERSITY

- Leading site: West China Hospital
  - One of the largest hospitals in China, performed 196,000 surgeries and 7.8 million out-patient services in 2021
  - Ranked #2 in the Fudan Best Hospital in China Rankings (2009-2020)

Principal Investigator: Prof. Weiming Li



- President of West China Hospital

Notes:

<sup>1</sup> Based on 2018 statistics

<sup>2</sup> <http://rank.cn-healthcare.com/rank/general-best>

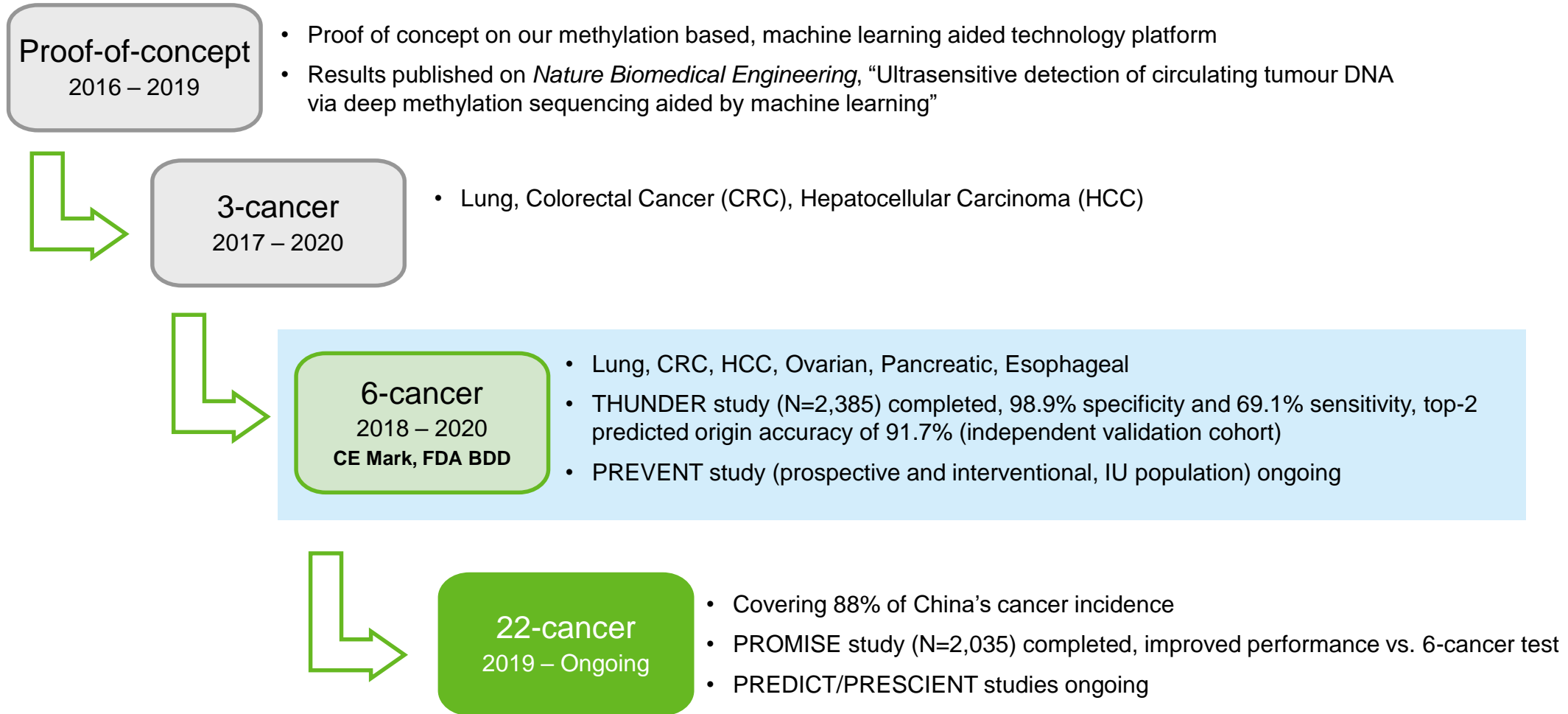
<sup>3</sup> CHCAMS

# Appendix 1

Early detection

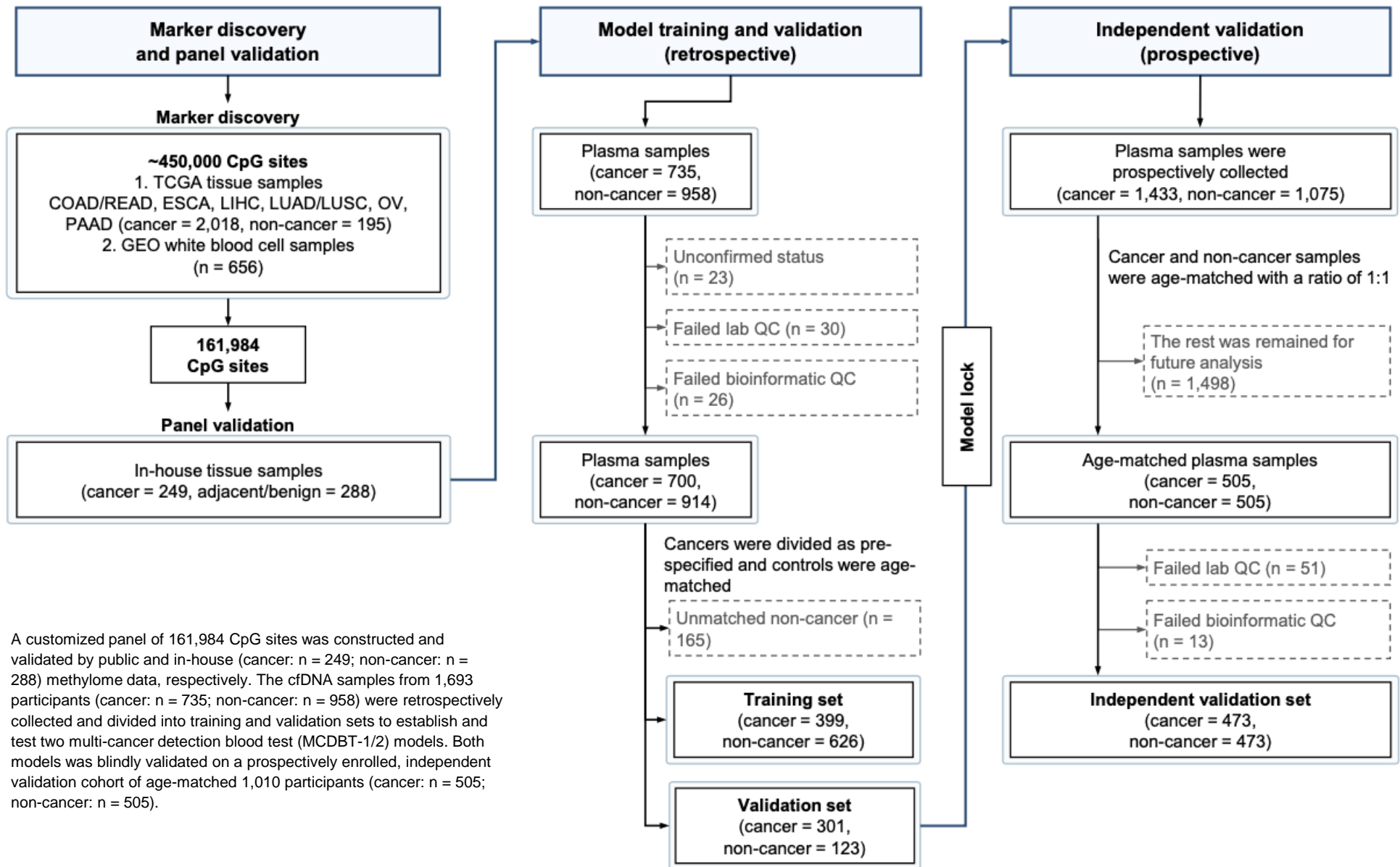
# Product Development Roadmap

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# 6-cancer test marker discovery and model training

## The THUNDER study, 2395 participants



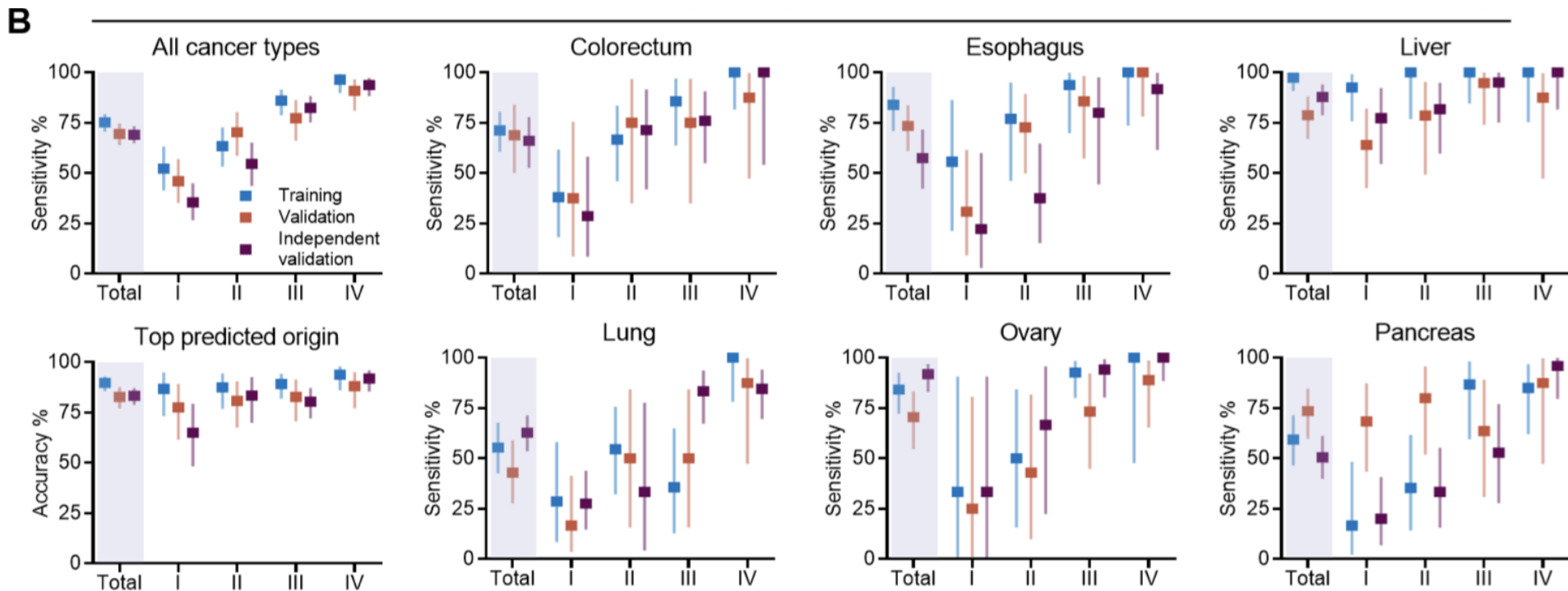
A customized panel of 161,984 CpG sites was constructed and validated by public and in-house (cancer: n = 249; non-cancer: n = 288) methylome data, respectively. The cfDNA samples from 1,693 participants (cancer: n = 735; non-cancer: n = 958) were retrospectively collected and divided into training and validation sets to establish and test two multi-cancer detection blood test (MCDBT-1/2) models. Both models were blindly validated on a prospectively enrolled, independent validation cohort of age-matched 1,010 participants (cancer: n = 505; non-cancer: n = 505).



# 6-cancer test, detection-of-cancer performance in case-control cohorts

## The THUNDER study

**Fig 3. Performance of the MCDBT-1/2 models. A.** Sensitivity, specificity, accuracy of top predicted origin, and accuracy of top two predicted origins. **B.** The overall sensitivity, accuracy of top predicted origin, and sensitivity stratified by cancer types reported by tumor stage.

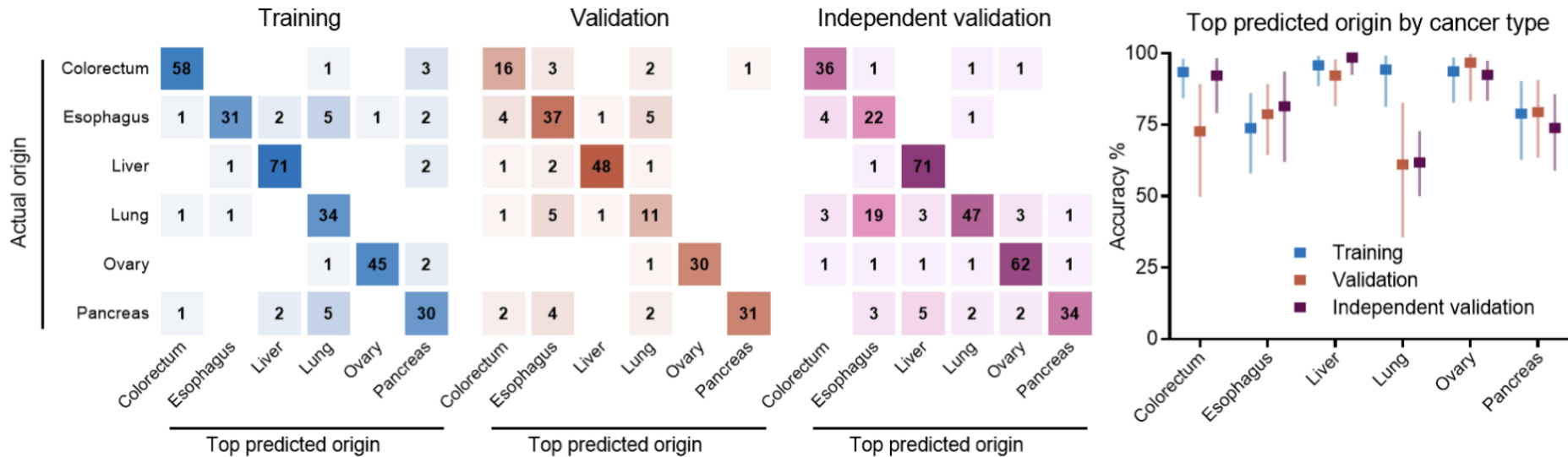


Data set	Specificity (%)	Sensitivity (%)	Accuracy of top predicted origin (%)	Accuracy of top two predicted origins (%)
Training set	99.7 (98.9-100.0)	75.2 (70.6-79.4)	89.7 (85.7-92.9)	94.7 (91.5-96.9)
Validation set	100.0 (97.0-100.0)	69.4 (63.9-74.6)	82.8 (77.0-87.6)	89.4 (84.5-93.3)
<b>Independent validation set</b>	<b>98.9 (97.6-99.7)</b>	<b>69.1 (64.8-73.3)</b>	<b>83.2 (78.7-87.1)</b>	<b>91.7 (88.2-94.5)</b>

# 6-cancer test, top-predicted-origin performance in case-control cohorts

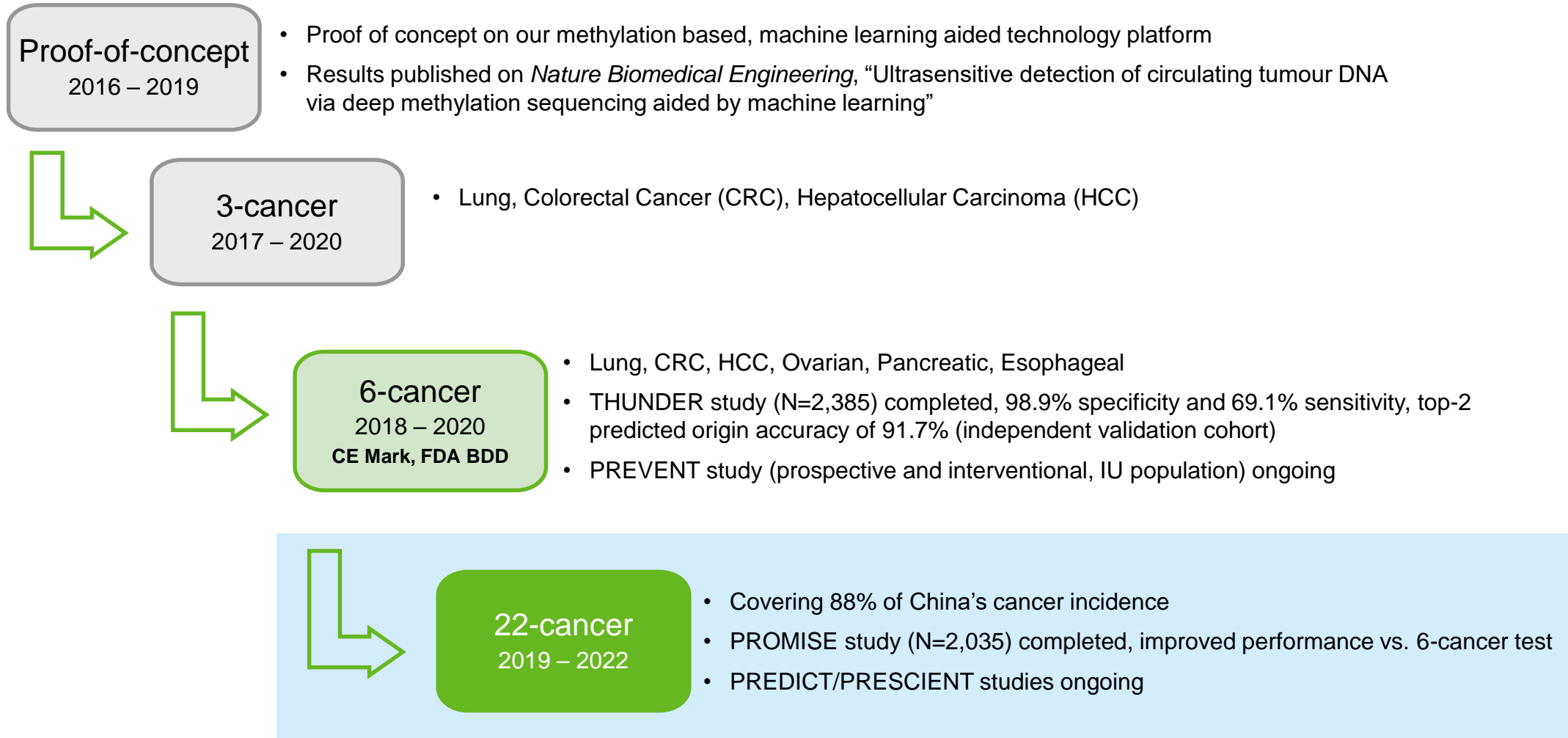
## The THUNDER study

**Fig 4. Top predicted origin for the MCBDT-1 model.** Confusion matrices representing the predicted origin in the training, the validation, and the independent validation sets.



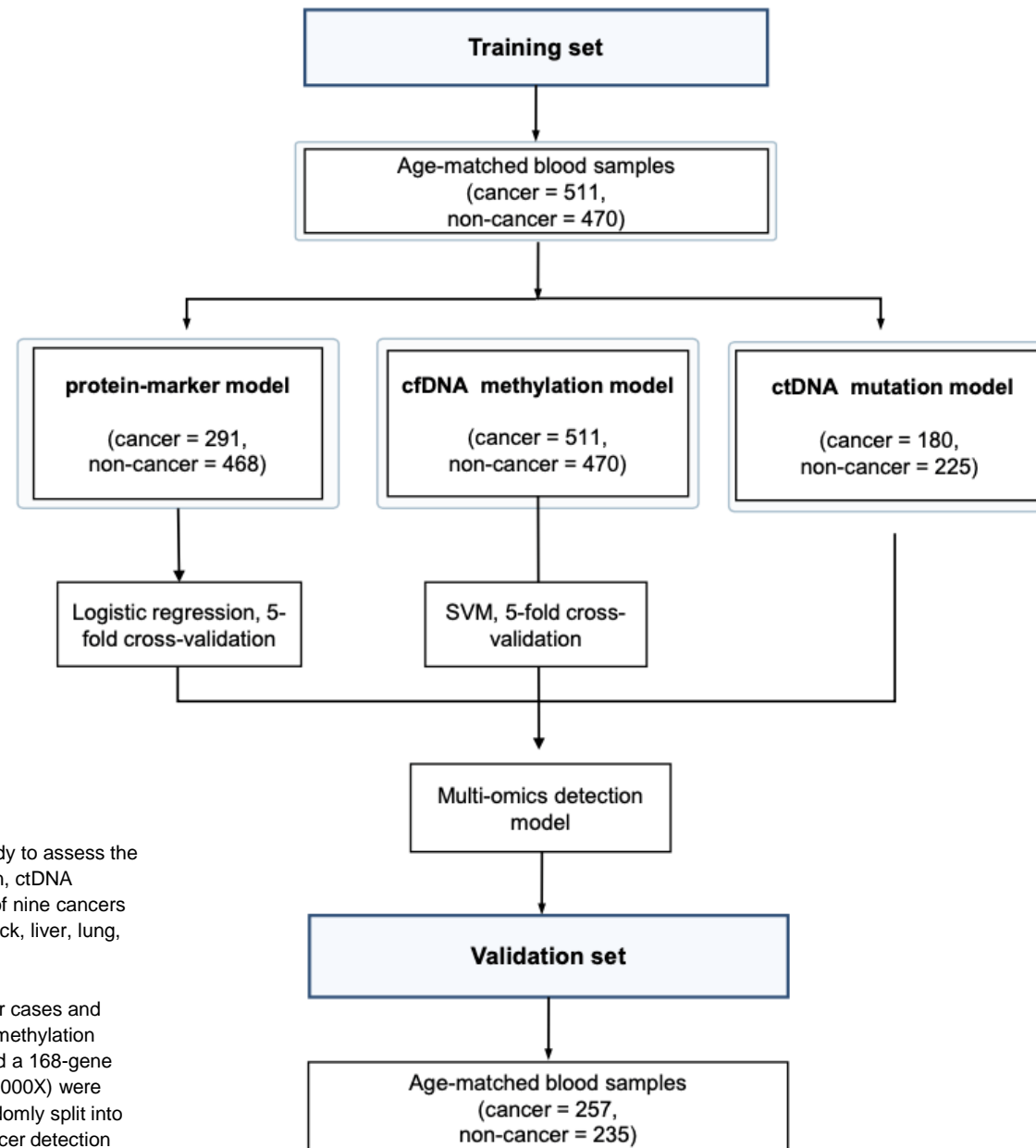
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# Product Development Roadmap



# 9-cancer test, multi-omics model

## The PROMISE study



PROMISE is a prospective multicenter case-control study to assess the performance of multi-omics including cfDNA methylation, ctDNA mutation and protein biomarkers in the early detection of nine cancers in the biliary tract, colorectum, esophagus, head and neck, liver, lung, ovary, pancreas and stomach.

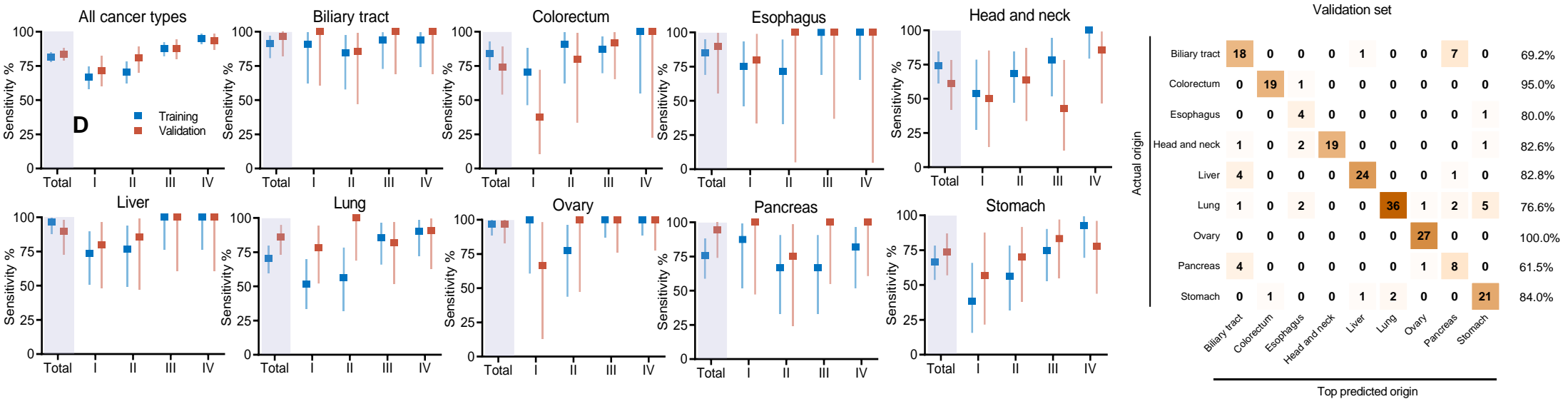
Blood samples were prospectively collected from cancer cases and non-cancer controls. A targeted cell-free DNA (cfDNA) methylation panel of ~490,000 CpG sites (1,000X) by ELSA-seq and a 168-gene mutation panel (35,000X, matched white blood cells:10,000X) were sequenced. Age-matched cases and controls were randomly split into training (n = 981) and test sets (n = 492). The multi-cancer detection blood test (MCDBT) models were developed in the training set and then validated in the test set.

# 9-cancer test multi-omics model performance

## The PROMISE study

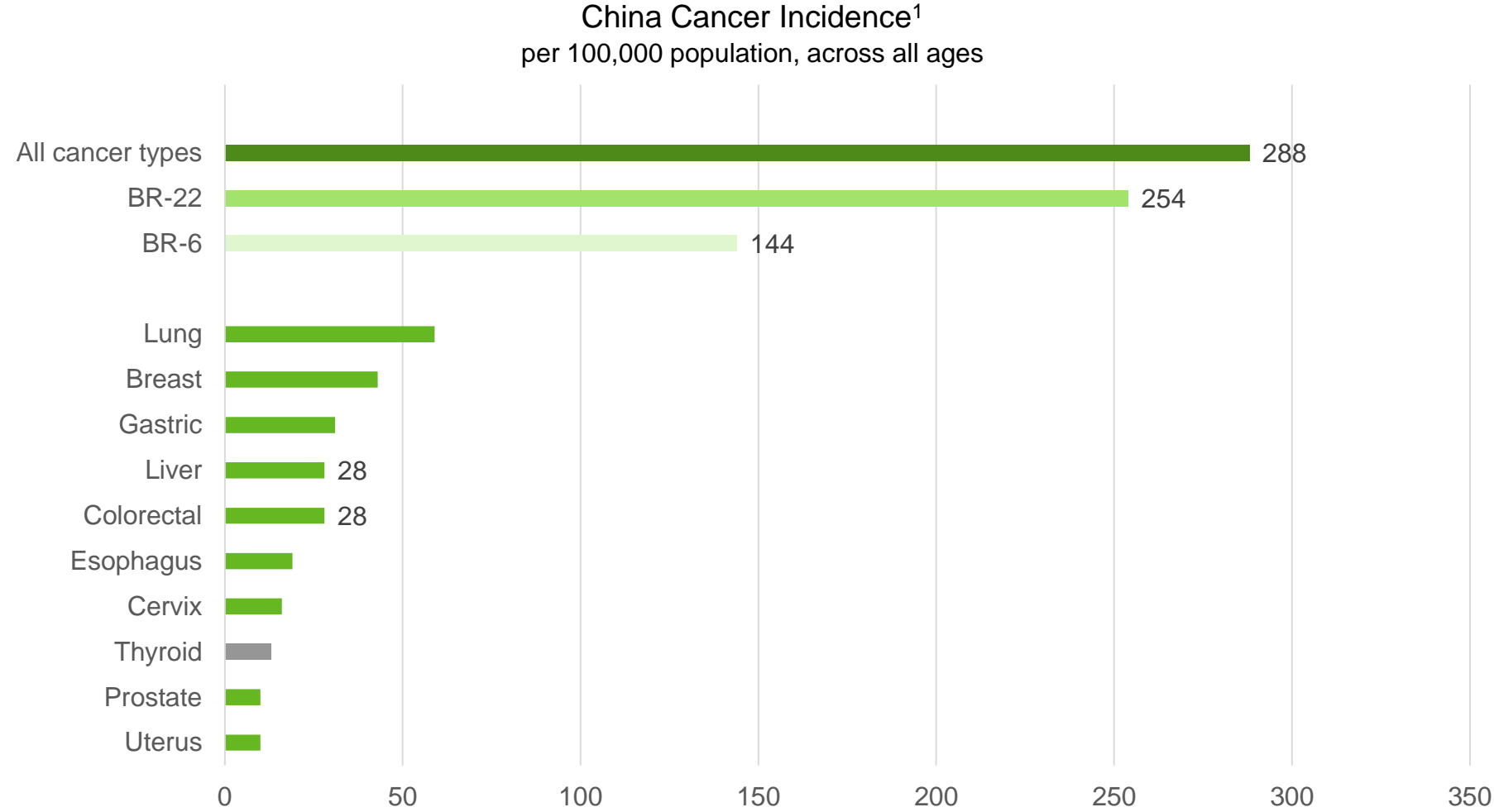
	Cancer (n)	Non-cancer (n)	Specificity (%)	Sensitivity (%)	Accuracy of top predicted origin (%)
Training	470	511	97.9% (96.1%-99.0%)	81.7% (78.1%-84.9%)	86.6% (83.0%-90.0%)
Validation	257	235	98.3% (96.6%-99.4%)	83.7% (79.0%-88.0%)	81.9% (76.0%-87.0%)

	Multi-omics	Methylation	Mutation	Protein
Specificity (95% CI)	98.3% (96.6%–99.4%)	99.1% (97.3%–99.8%)	99.6% (97.9%–100.0%)	99.6% (98.7%–100.0%)
Sensitivity (95% CI)	83.7% (78.6%–88.0%)	79.0% (73.5%–83.8%)	49.4% (41.9%–57.0%)	47.8% (40.8%–54.9%)



- PROMISE demonstrated 83.7% sensitivity and 98.3% specificity for 9 cancers
- Methylation contributed >90% of the total sensitivity, while protein and mutation collectively provided <10% additional positive detections

# Burning Rock's 22-cancer test covers 88% of China's cancer incidence



Notes:  
<sup>1</sup> Incidence data per "2018 China cancer registry annual report ", J He et al., ISBN 978-7-117-28585-8  
<sup>2</sup> Final number of cancer types subject to development progress

# Leadership in multi-cancer early detection

First-in-class, high entry-barrier, multi-year efforts

## Challenges

## BNR position

1

### Technology

Low amount of cancer signal  
in the circulating bloodstream, much more  
challenging compared to tissue

### Proprietary chemistry and algorithm

- On par with global leader, competitive sensitivity in earlier stages for certain cancers
- Multi-year lead vs. China peers (most showing liver-cancer and colon-cancer data only)

2

### Clinical

Large, multi-year studies required  
from case-control to intend-to-use population, from  
observational to interventional (e.g. CCGA study:  
15,254 participants, 8,584 with cancer, 6,670  
without cancer)

### Sponsorship from top physicians

- Catching up with global leader, to improve specificity and tissue-of-origin performance through large clinical studies
- Multi-year lead in China as the only company that has launched studies with over 10,000+ subjects

3

### Regulatory

First-in-class  
with no established regulatory pathway

### Leading regulatory capability in China

- Exploring possible pathway, leveraging experience through the country's first NMPA-approved NGS kit

4

### Commercial

Unprecedented product

### Multi-pronged approach

- Initially working with hospitals' health check-up departments, leveraging synergy from in-hospital therapy selection business

# Appendix 2

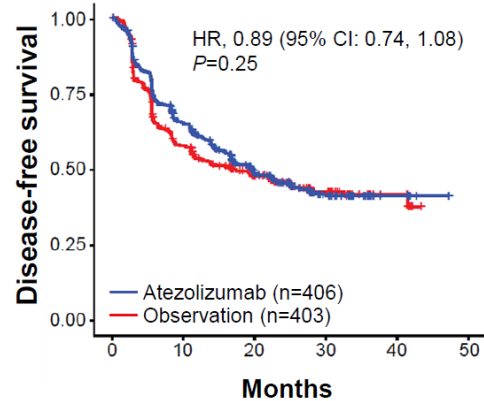
MRD



# How do MRD studies advance utility

Example 1: IMvigor010, enrich the high-risk group and "tune-up" adjuvant treatment

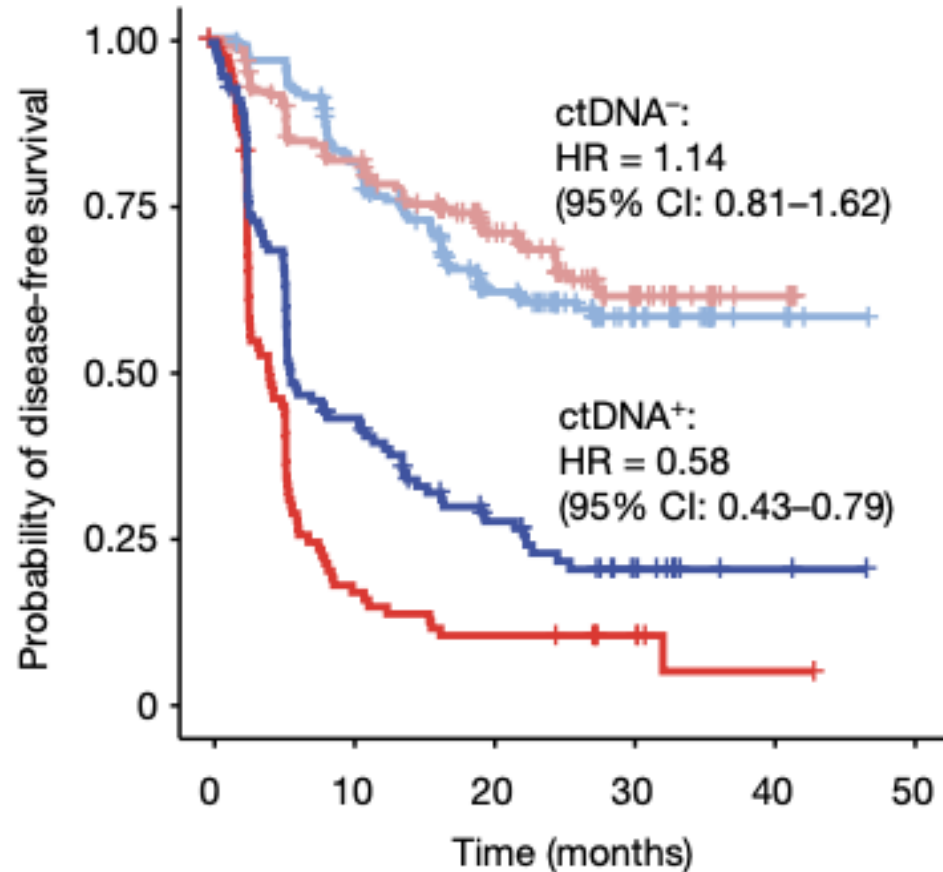
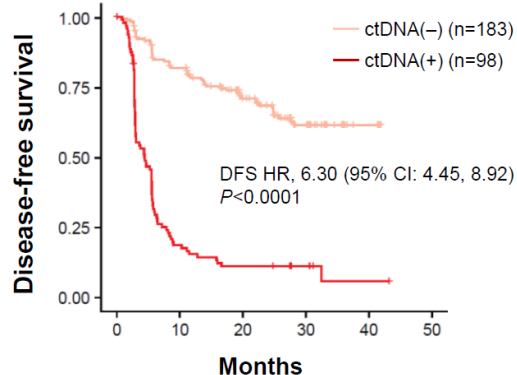
ITT



Atezo, MIUC Adjuvant Therapy  
"All comers" demonstrated NO efficacy  
TMB/PD-L1 showed NO prediction



Observation arm



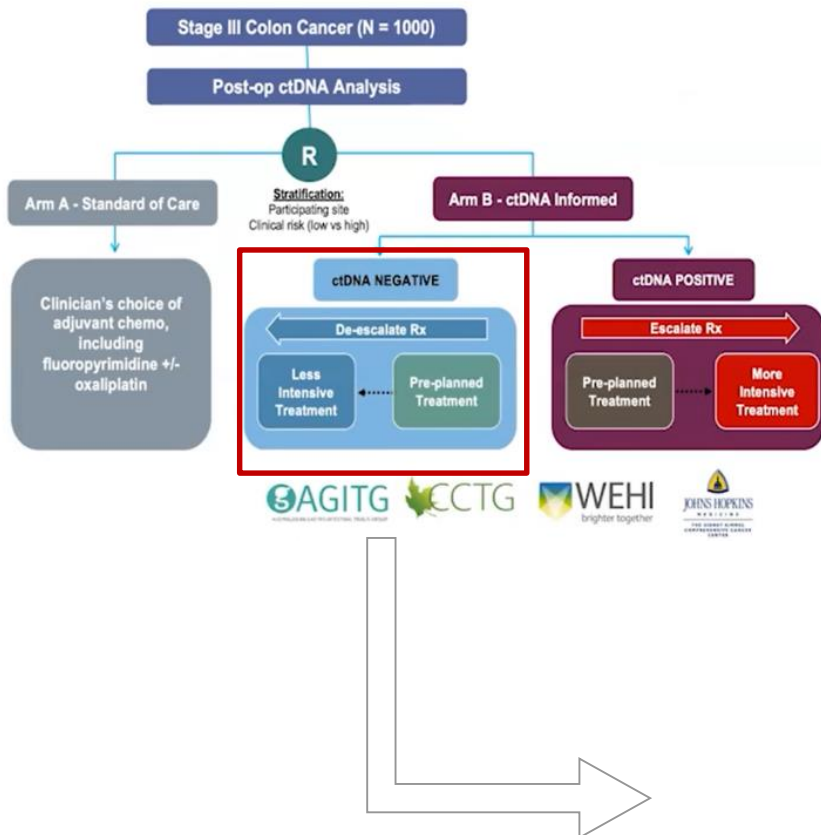
Indeed, only baseline MRD+ pts showed benefit

Landmark MRD+ pts (39%) had worse prognosis  
Maybe only those patients can benefit?

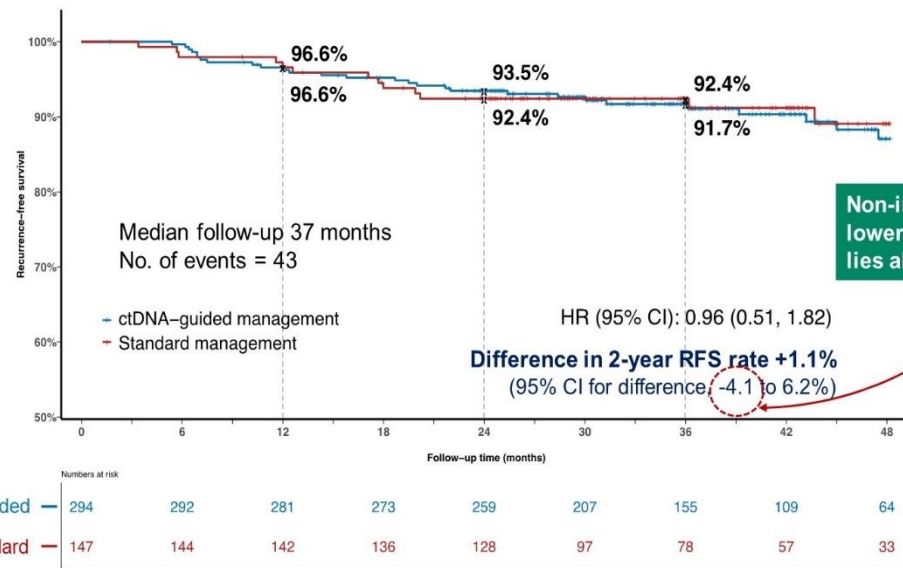
# How do MRD studies advance utility

Example 2: Dynamic, identify low-risk patients and “tune-down” adjuvant treatment

## DYNAMIC-III

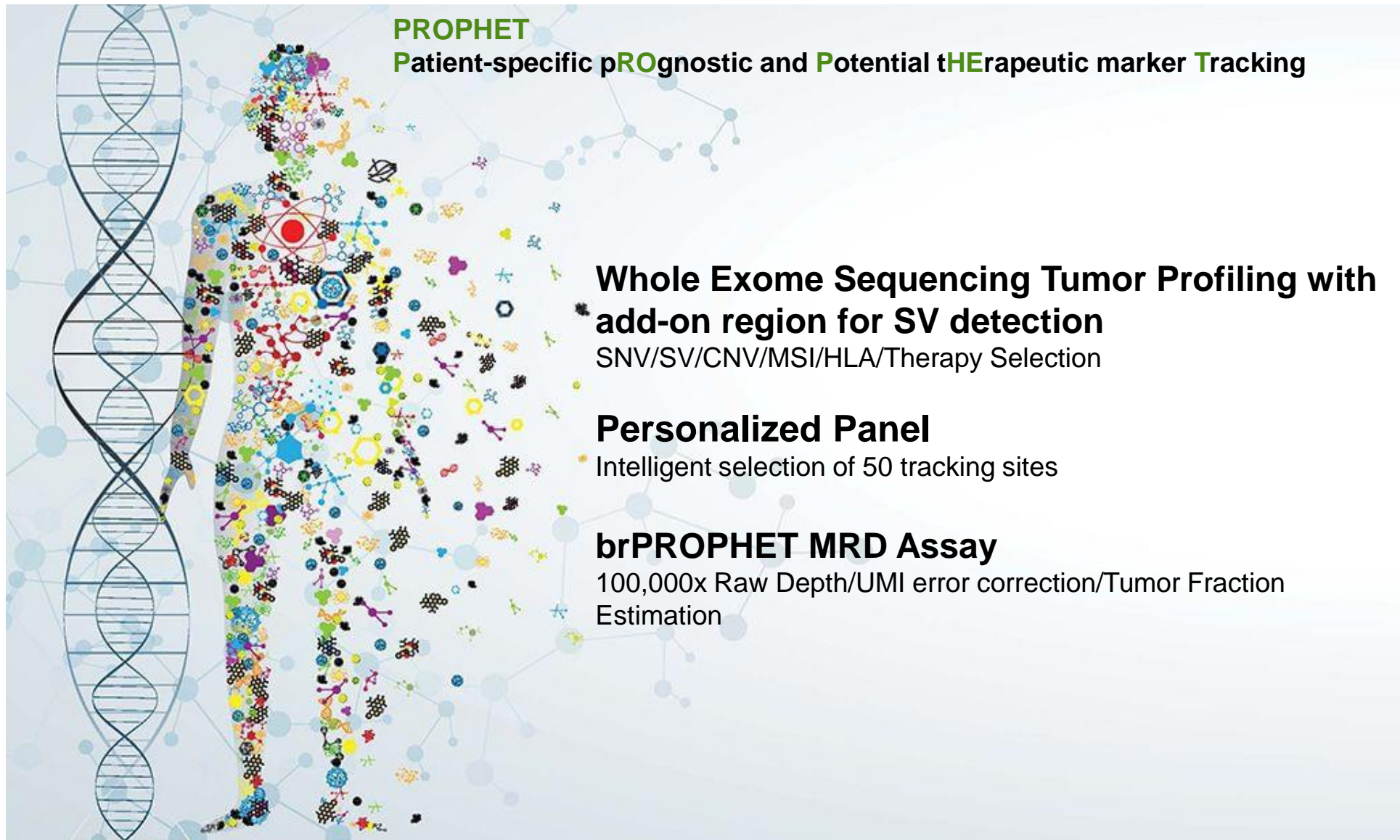


## ctDNA-guided vs standard



The ctDNA-guided MRD- group had fewer patients with adjuvant chemotherapy than the standard group (15% vs. 29%) with non-inferiority of 3-year RFS (92.4% vs 91.7%)

# brPROPHET™ – Burning Rock's MRD solution



**PROPHET**  
Patient-specific pROgnostic and Potential tHERapeutic marker Tracking

**Whole Exome Sequencing Tumor Profiling with add-on region for SV detection**  
SNV/SV/CNV/MSI/HLA/Therapy Selection

**Personalized Panel**  
Intelligent selection of 50 tracking sites

**brPROPHET MRD Assay**  
100,000x Raw Depth/UMI error correction/Tumor Fraction Estimation

# Gastric cancer cohort publication at AACR 2023



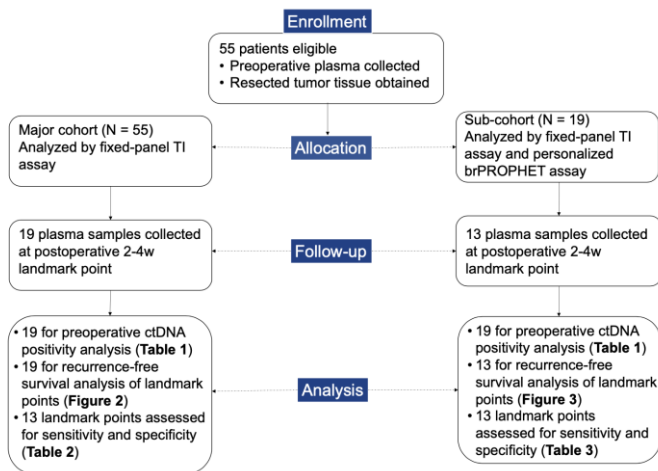
## Circulating tumor DNA - based molecular residual disease predicts relapse in patients with resectable gastric cancer

Pei Xue<sup>1</sup>, Yanfei Shao<sup>1</sup>, Xueliang Zhou<sup>1</sup>, Haiyan Li<sup>2</sup>, Yang Wang<sup>2</sup>, Chenyang Wang<sup>2</sup>, Hao Zhang<sup>2</sup>, Bing Li<sup>2</sup>, Shuo Shi<sup>2</sup>, Haiwei Du<sup>2</sup>, Jing Sun<sup>1</sup>  
 1. Department of General Surgery, Ruijin Hospital, Shanghai Jiao Tong University, Shanghai, China  
 2. Burning Rock Biotech, Guangzhou, China

2023 AACR  
 #1037



### Study cohort



### Personalized assay significantly out-performs fixed panels

The ctDNA+ rate of preoperative samples detected by fixed panel and personalized brPROPHET™ assays

ctDNA+ rate	Stage I	Stage II	Stage III	Overall
Fixed panel	0% (0/4)	0% (0/3)	58.3% (7/12)	36.8% (7/19)
brPROPHET	100% (4/4)	66.7% (2/3)	91.7% (11/12)	89.5% (17/19)

### Postoperative prognosis

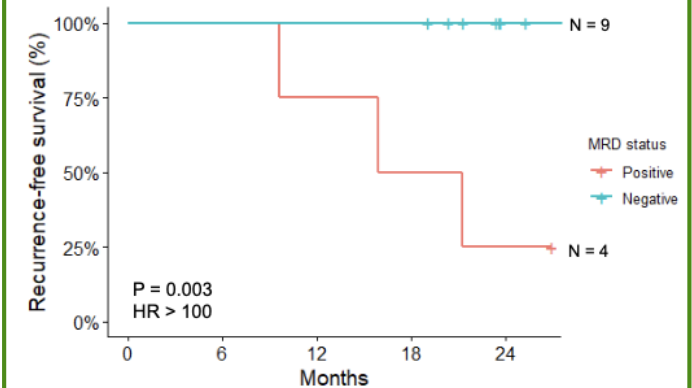


Table 3. The performance of MRD status detected by brPROPHET in predicting tumor recurrence.

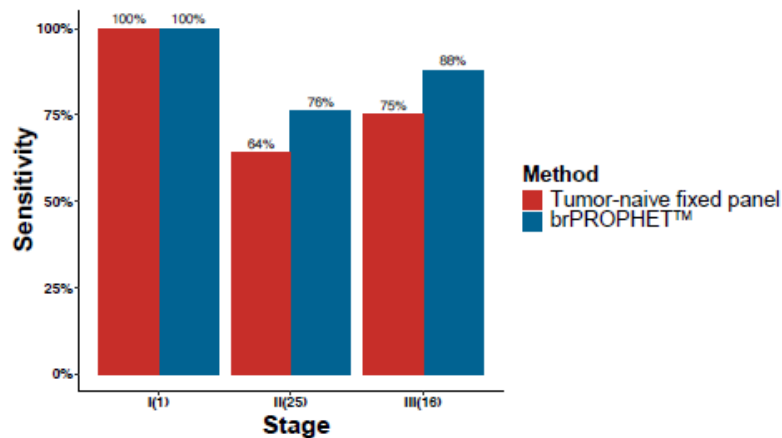
MRD status	Tumor recurrence		PPV=75%
	+	-	
+	3	1	NPV=100%
-	0	9	
		Sensitivity=100%	Specificity=90%

PPV, positive predictive value; NPV, negative predictive value.

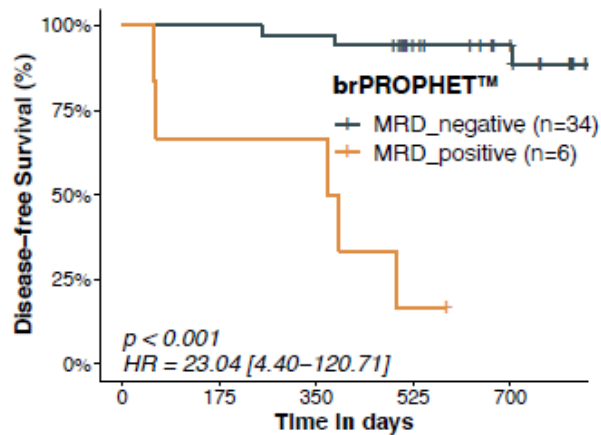
# Colorectal cancer cohort publication at AACR 2022

Session OPO.PR02.01 - Clinical Prevention, Early Detection, and Interception

## 5917 - Patient-specific tumor-informed circulating tumor DNA (ctDNA) analysis for postoperative monitoring of patients with stages I-III colorectal cancer (CRC)

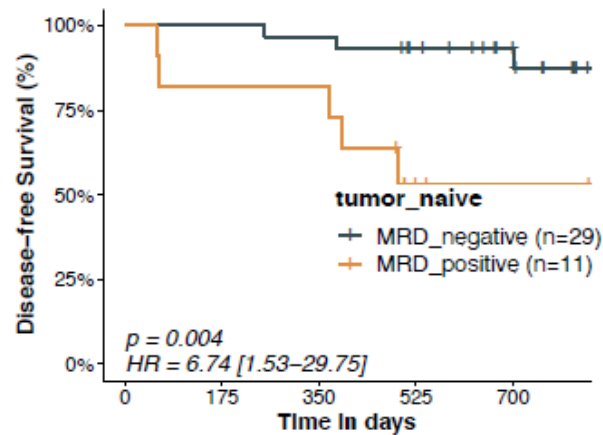


*brPROPHET™ demonstrated superior sensitivity and specificity to fixed panel in pre-operative ctDNA detection and post-operative MRD calling among relapsed patients*



Number at risk

—	34	34	33	25	17
—	6	4	4	1	0



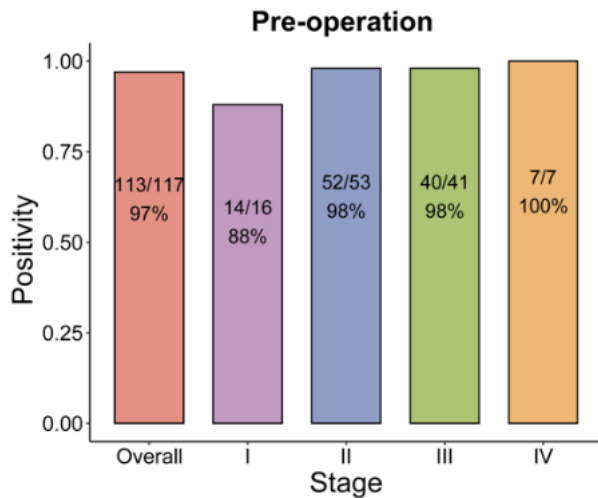
Number at risk

—	29	29	28	24	16
—	11	9	9	2	1

# Second colorectal cancer cohort publication at ASCO GI 2023

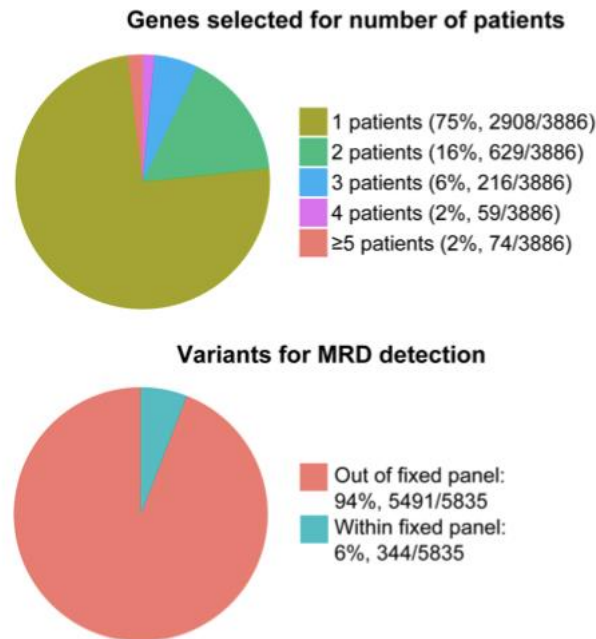
## brPROPHET™ has high detection sensitivity

Preoperative ctDNA was detected in 97% (113/117) of the patients with 88% (14/16), 98% (52/53), 98% (40/41), and 100% (7/7) in stage I, II, III and IV, respectively



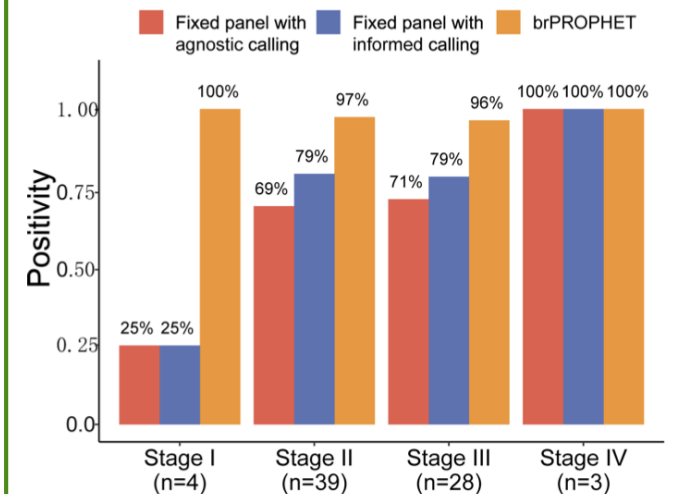
## Most mutation variants fall outside of fixed panels

Only 6% of designed variants were included in the fixed panel. 75% of genes selected for panel design were private to a specific patient.



## brPROPHET™ significantly out-performs fixed panels

Preoperative ctDNA was detected in 97% (113/117) of the patients with 88% (14/16), 98% (52/53), 98% (40/41), and 100% (7/7) in stage I, II, III and IV, respectively



**Patients:** A total of 117 patients (stage II/III 53 [45.3%] / 41 [35.0%]) who received surgery were analyzed. A subset of 74 patients were analyzed for comparisons of different methods.

**Samples:** Tumor tissue samples were collected at the surgery. Plasma samples collected at baseline, landmark 7-day and 1-month, and longitudinal points were analyzed.

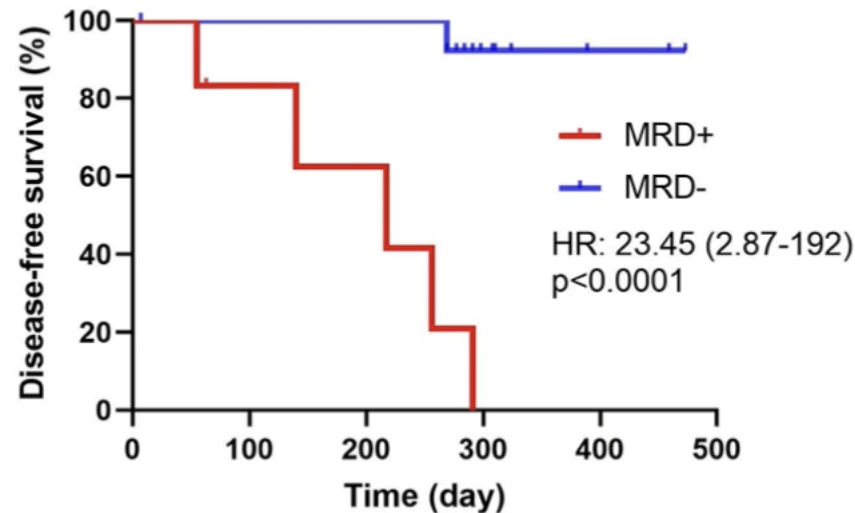
Source: Cao et al., Patient-specific tumor-informed circulating tumor DNA analysis for molecular residual disease detection in surgical patients with stages I-IV colorectal cancer, ASCO GI 2023

# Pancreatic cancer cohort publication at ASCO GI 2023

Table 1: ctDNA detection at serial timepoints

	Baseline (Day 0)	Timepoint A (Day 7)	Timepoint B (Day 30)	Timepoint C (During AT)	Follow-ups
<b>Positive</b>	20	2	1	2	4
<b>Negative</b>	0	16	9	12	5
<b>Positive Rate</b>	<b>100%</b>	<b>11.1%</b>	<b>10%</b>	<b>14.3%</b>	<b>44.4%</b>

Figure 1: Longitudinal MRD detection is associated with shorter disease-free survival



**Patients:** A total of 20 patients (stage I/II 10 [50.0%] / 9 [45.0%]) were analyzed. 13 (65.0%) patients were treated with adjuvant therapy (AT) after surgery.

**Samples:** Tumor tissue samples were collected at the surgery. Plasma samples collected at baseline (n=20), landmark 7-day (n=18) and 1-month (n=10), and longitudinal points (n=23) were analyzed. Patients were followed for a median of 302 days. 39


# Appendix 3

Therapy selection



# NMPA approved NGS panels

NMPA approved testing kits by major NGS-focused companies<sup>1</sup>

	First NMPA-approved kit	Second NMPA-approved kit
	EGFR, ALK, BRAF, KRAS Approved in Jul <b>2018</b> <u>First approved NGS kit in China</u>	EGFR, KRAS, MET, ERBB2, BRAF, PIK3CA, ALK, ROS1, RET Approved in Mar <b>2022</b>
Novogene 诺禾	EGFR, KRAS, BRAF, PIK3CA, ALK, ROS1 Approved in Aug <b>2018</b>	
Geneseeq 世和	EGFR, ALK, ROS1, BRAF, KRAS, ERBB2 Approved in Sep <b>2018</b>	
BGI 华大	EGFR, KRAS, ALK Approved in Aug <b>2019</b>	
Gene+ 吉因加	EGFR, KRAS, ALK Approved in Dec <b>2019</b>	
Genetron 泛生子	EGFR, KRAS, BRAF, ERBB2, PIK3CA, ALK, ROS1, MET Approved in Feb <b>2020</b>	
Genecast 臻和	KRAS, NRAS, BRAF, PIK3CA Approved in Mar <b>2021</b>	
3DMed 思路迪		

Highlights on our second NMPA-approved kit

- Only 30ng DNA input required, applicable to small tissue samples
- First NMPA approved NGS kit with CNV<sup>2</sup> mutation type, with MET exon14 skipping

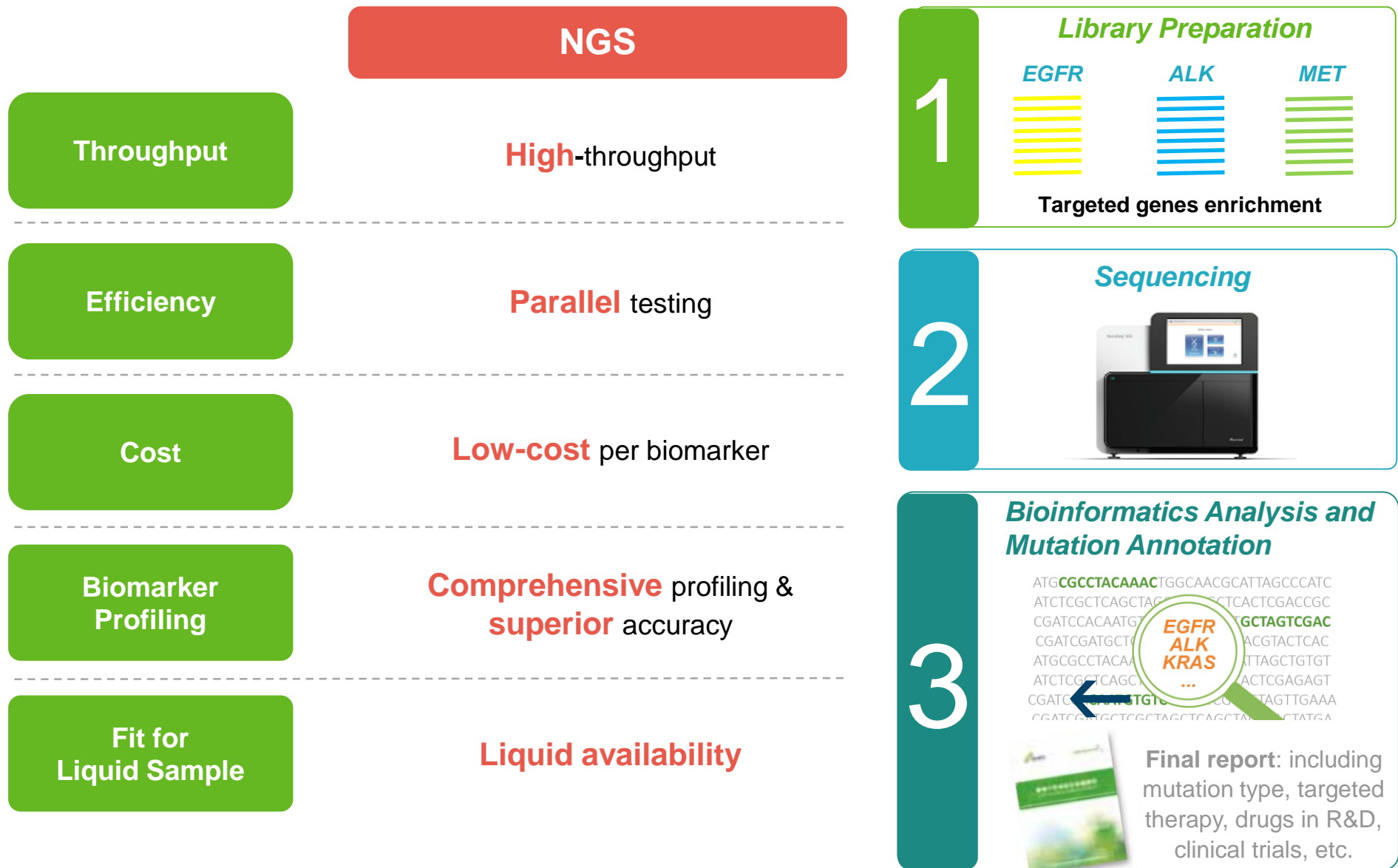
Notes:

<sup>1</sup> The list is not exhaustive. A total of 13 kits have been approved by the NMPA as of the date of this presentation

<sup>2</sup> Copy number variation

# NGS testing

Diagnostics companies focus on steps 1 and 3



# Leading liquid-biopsy product in China, with globally competitive performance

## Demonstrated in high-impact analytical validation study

SEQC2  
Study  
Overview

### MAQC/SEQC Consortium Projects – An Overview

- An FDA-led community-wide consortium effort to assess technical performance and application of emerging technologies (e.g., genomics).



### Issues and Study Objectives

- FDA approved several NGS tests with sensitivity for AF ~5%
- Hundreds lab developed tests (LDT): sensitivity ~ 2-10%
- FDA approved ctDNA tests with sensitivity for AF ~0.3%



## Evaluating the analytical validity of circulating tumor DNA sequencing assays for precision oncology

- False positive rate estimate through known negatives
- All of them by VAF ranges:
  - 0.1 - 0.5%, 0.5 - 2.5%, >2.5%
  - Finer VAF ranges for sensitivity: 0.1 - 0.2%, 0.2 - 0.3%, 0.3 - 0.5%
- Evaluate the impact of DNA input amount
  - Three levels of input for Ef: 10ng, 25ng, 50ng
- Evaluate the impact of synthetic plasma (DNA extraction)
  - Qubit HS calibration and quantification
  - Calculate extraction yield

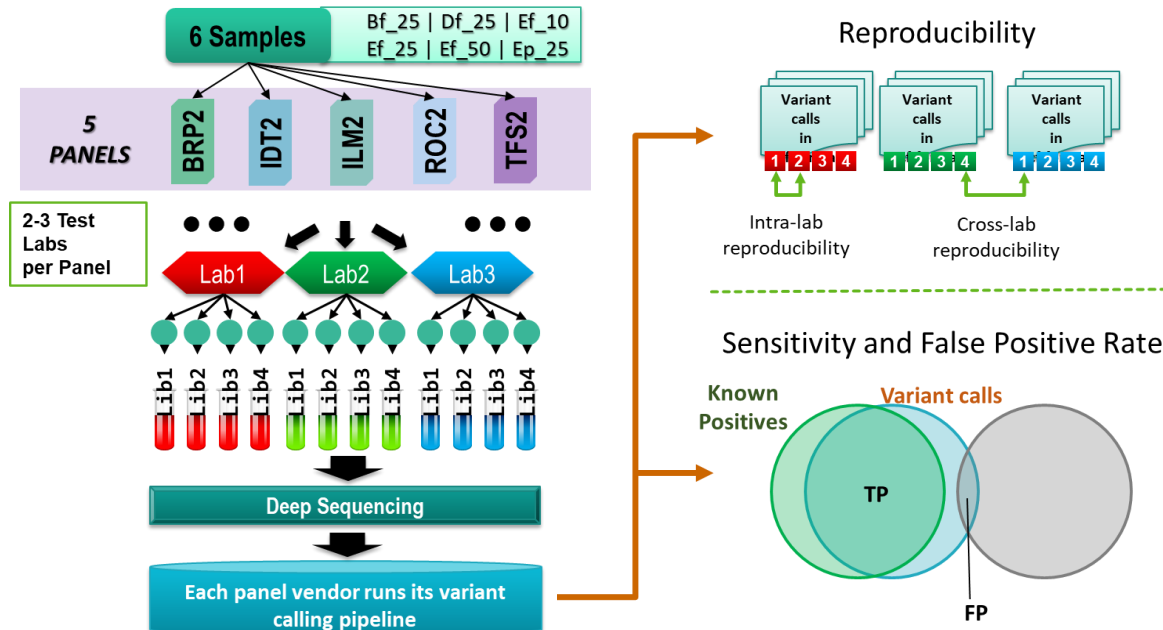
- Enzymatic fragmentation
  - better ligation efficiency
- Gel-based size selection (160bp-180bp) to mimic cfDNA
- 1ng/ul to mimic concentration after DNA extraction from plasma
- Ep: 40ng/ml Ef in synthetic plasma

- BRP2:** Burning Rock Dx LungPlasma v4
- IDT2:** IDT xGen Non-Small Cell Lung Cancer
- ILM2:** Illumina TruSight 170 with UMI
- ROC2:** Roche AVENIO ctDNA Expanded Kit
- TFS2:** Thermo Fisher Oncomine Lung cfDNA Assay

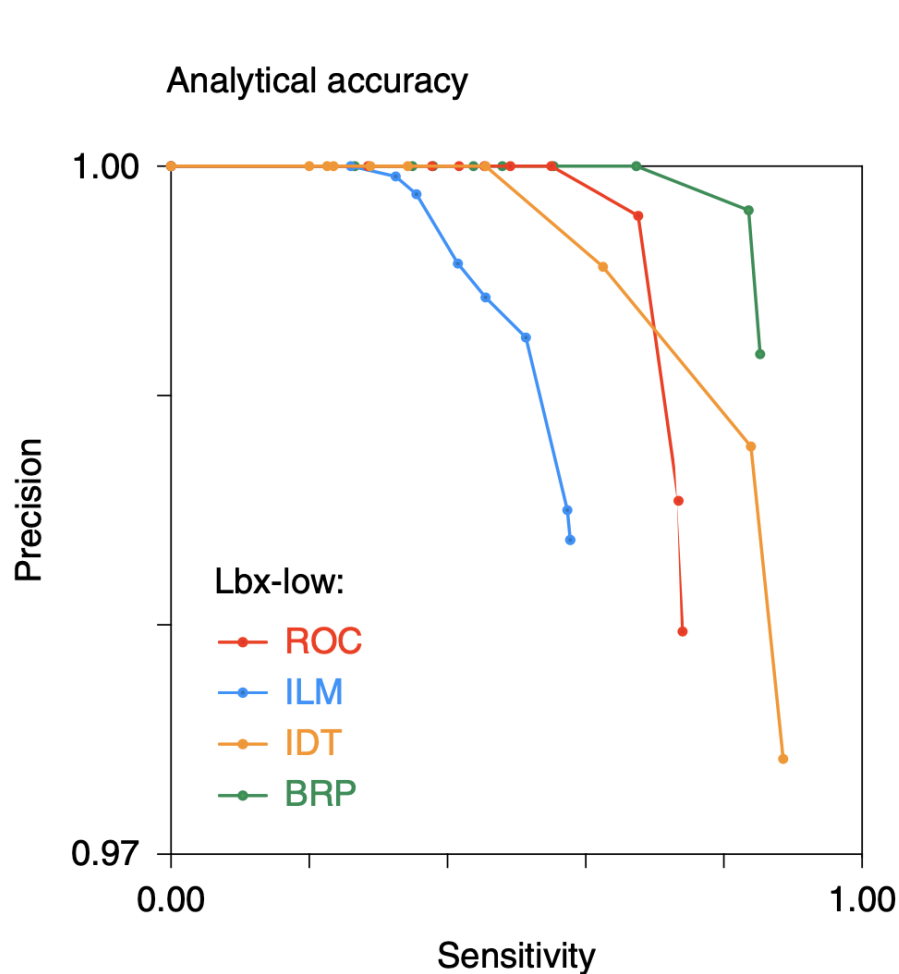
Liquid  
Biopsy

# Participating assays and study design

Name	Vendor	ctDNA assay	Sequencing platform	Target genes	Reportable region (kb)	Coding (kb)	CTR (kb)	Negatives (× 1,000)	Variants
<b>ROC</b>	Roche Sequencing Solutions	AVENIO ctDNA (Expanded Kit)	Illumina NextSeq	77	161.7	140.2	103.8	47.1	189
<b>ILM</b>	Illumina	TruSight Tumor 170 + UMI	Illumina NovaSeq	154	501.0	390.1	338.4	133.0	574
<b>IDT</b>	Integrated DNA Technologies	xGen Non-small Cell Lung Cancer	Illumina NovaSeq	24	110.1	93.2	76.5	39.3	130
<b>BRP</b>	Burning Rock Biotech	Lung Plasma v4	Illumina NovaSeq	168	226.9	148.5	125.1	53.4	229
<b>TFS</b>	Thermo Fisher Scientific	Oncomine Lung cfDNA assay	Ion Torrent S5 XL	11	1.9	1.6	1.3	0.8	5



# Overall analytical accuracy and specificity

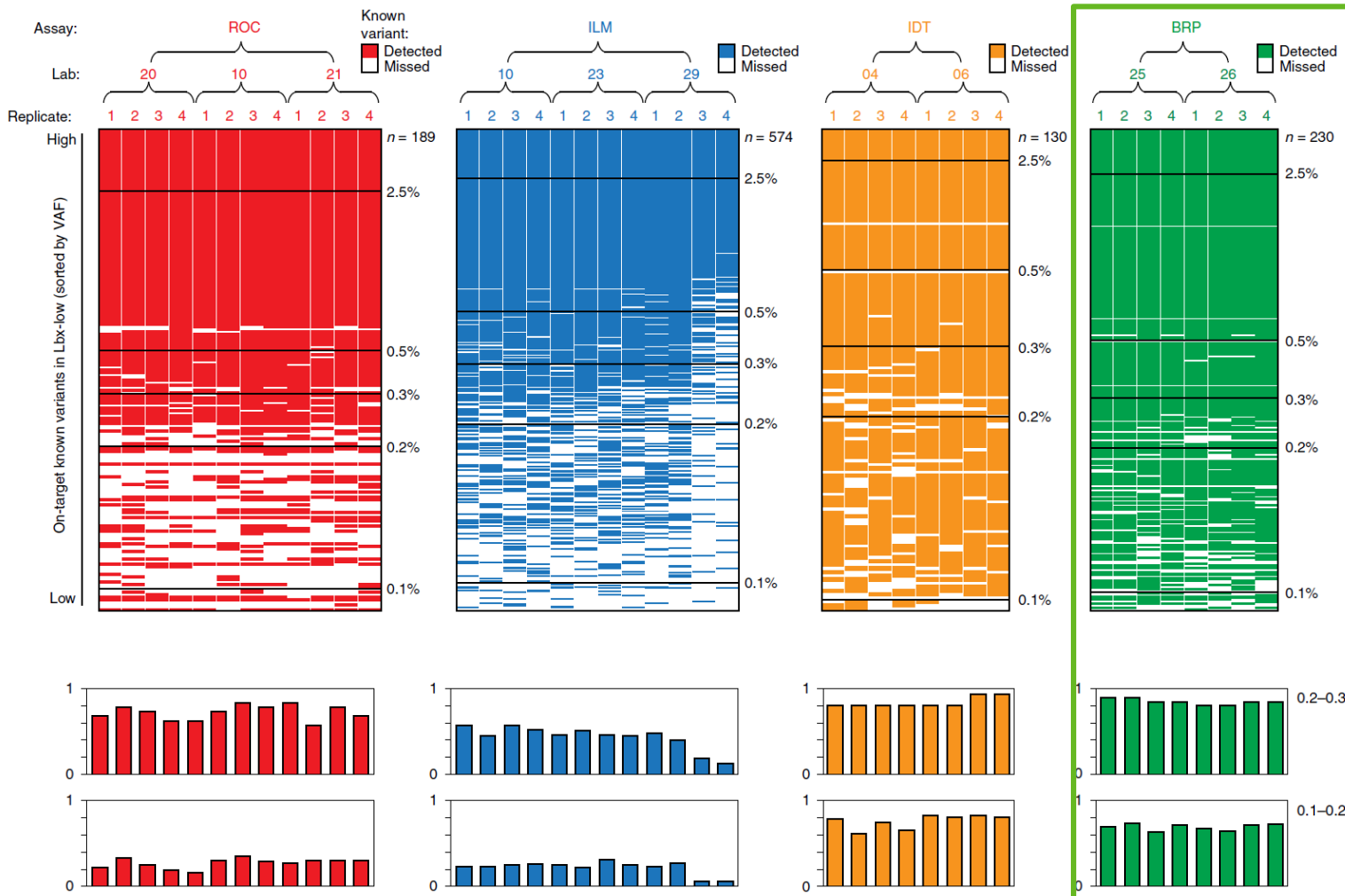


Assay	Known negatives (kb)	FPs per replicate (mean [range])	FP-rate (FP / kb) at specified VAF threshold		
			> 0%	> 0.1%	> 0.5%
ROC	47.1	2.91 [1-6]	0.061	0.044	0.000
ILM	133	5.25 [2-10]	0.039	0.039	0.008
IDT	39.3	2.75 [0-6]	0.070	0.057	0.000
BRP	53.4	1.65 [0-5]	0.030	0.007	0.000

The analytical accuracy was measured by **Precision-Sensitivity** plot (25ng LBx-Low)  
 The false positive rates were computed by FP/kb region.  
 Once different VAF threshold increases, FP rates dropped further.

“To compare the accuracy of the participating ctDNA assays, we generated precision recall curves, ranking known variants and FPs according to their observed VAFs. **For Lbx-low samples at 25ng input, BRP was the most accurate assay, with roughly equivalent sensitivity but superior precision to IDT** (Fig. 4b and Supplementary Fig. 4c).”

# Performance – Sensitivity



- LBx-low (25 ng input) replicates in each participating assay in different expected VAF bin.

**“The most sensitive assays (IDT and BRP) achieved sensitivity greater than 0.90 for variants with 0.3–0.5% VAF; however, no assays reached this mark for variants with 0.2–0.3% or 0.1–0.2% VAF (Fig. 4a).”**

“The performance characteristics of the assays evaluated here were broadly similar to what has been reported by several ctDNA sequencing providers (based on internal testing) that did not participate in this study. **During validation of the Guardant360 CDx hybrid capture assay, variants were detected with high sensitivity (~94%) at VAF  $\geq$  0.4%, declining to ~64% among variants with VAF ranging from 0.05% to 0.25%.** **FoundationACT showed ~99% sensitivity for SNVs with VAF > 0.5%, ~95% for 0.25%–0.5% VAF and ~70% for 0.125–0.25% VAF.**”