



Burning Rock Biotech Limited

1Q2022 results presentation

BNR US Equity
31 May 2022

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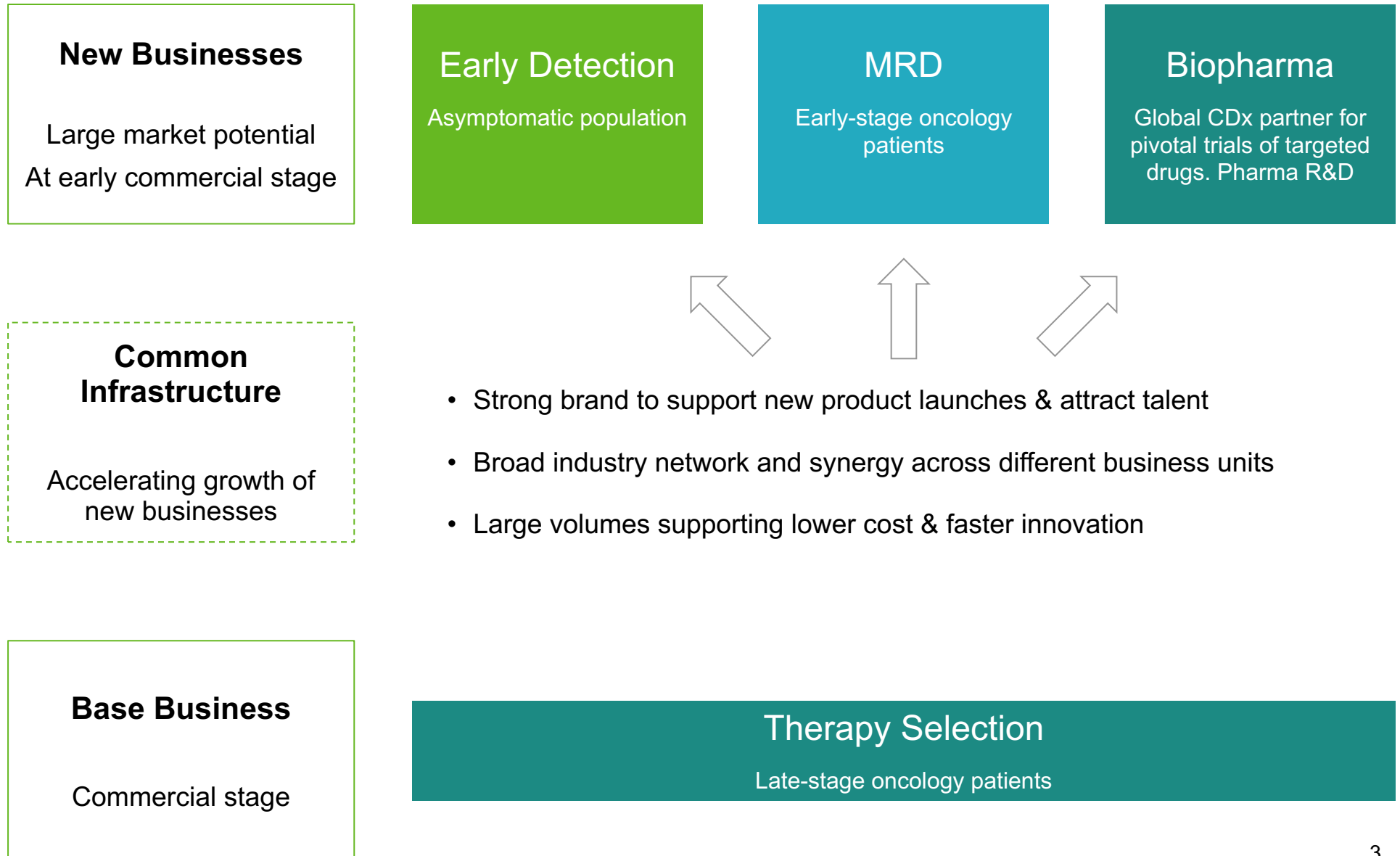
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Our value-building blocks

Extending leadership in NGS-based precision oncology from late-stage patients to earlier stages, driving the next phase of growth



Recent progress

In-hospital growth despite Covid impact, MRD coming live, pharma revenue strong ramp

Industry

- China's 14th five-year development plan for the life sciences industry released by NDRC¹ in May. NGS and cancer early detection are featured as key development areas

Therapy Selection, MRD

- Continued growth through i) market share gain via in-hospital strategy and ii) new product ramp-up
1Q volume +42% YoY (in-hospital +83%), Apr volume +15% despite heavy Covid impact (in-hospital +60%)
New products contributed c.7% of central-lab revenues in Mar
- MRD data release at AACR for NSCLC² and CRC³
- MRD commercial launch in Mar, sales generation chiefly from NSCLC and CRC indications

Early Detection

- Data release at AACR on analytical validation
- Pipeline progress continues. PROMISE study for 9-cancer reading out 2022; PREDICT study >50% enrolled.
- Commercial progress continues, with a few hospitals having completed product on-boarding and generating revenues

BR Liquid Biopsy Conference

A 2-day online session in Apr chaired by Prof. Jia Fan, Jinming Yu and Xu Zhang, with over 150 oncologist participating as speakers or panelists

Released the Consensus on NGS Clinical Report Interpretation

Pharma

- Continued revenue ramp
in 1Q22, +303% YoY. Strong backlog progress of RMB59m new contract value signed during 1Q22, +125% YoY

Notes:

¹ National Development and Reform Commission

² Non-small cell lung cancer

³ Colorectal cancer

LBO – the Liquid Biopsy of Oncology conference



A conference dedicated to liquid biopsy advancement in oncology

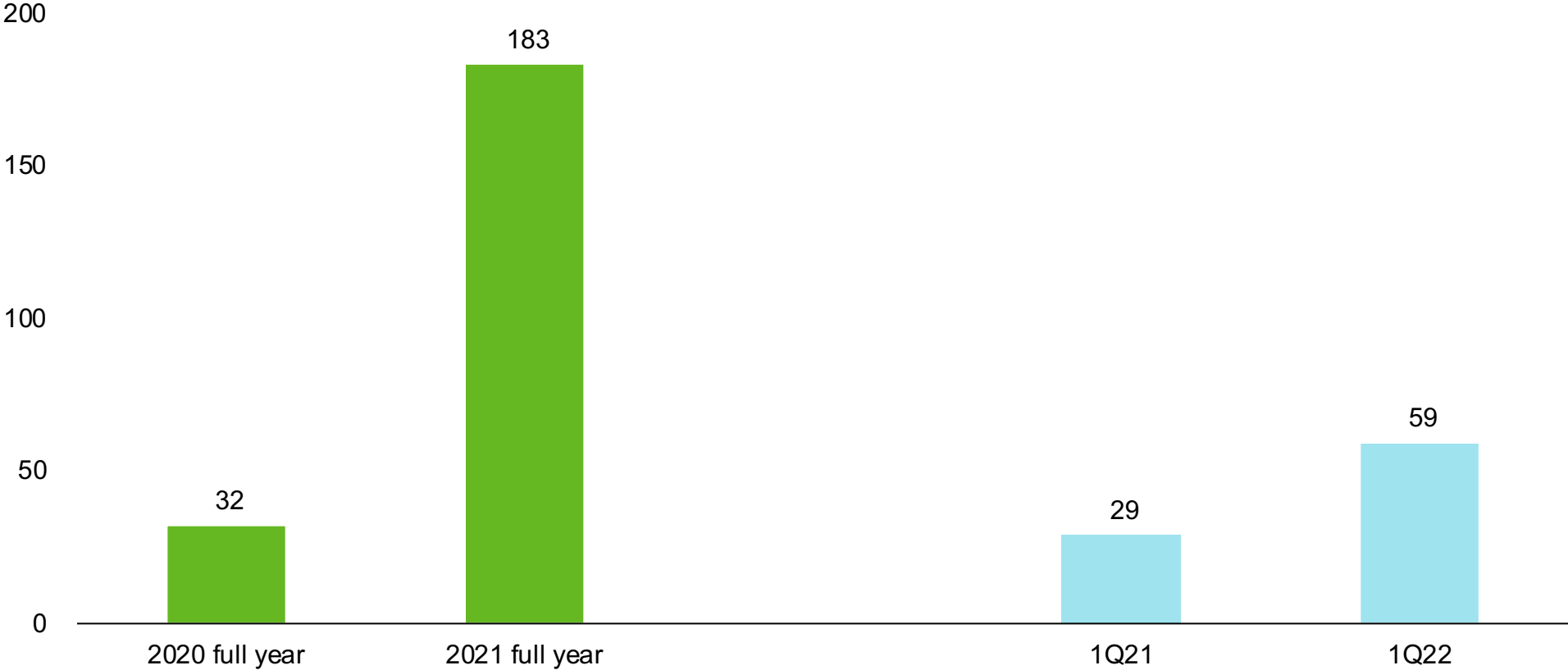
- 8th – 9th Apr, a two-day virtual event, with a total audience of 36,659, fully organized and sponsored by Burning Rock
- Keynote speeches and roundtable discussions on cancer early detection, MRD, CDx and diagnostics registration pathway
- 150+ top oncologists invited as speakers and panelists, including 3 fellows from China Academy of Sciences / Engineering and 7 heads of hospitals
- Collaborated with the CSCO Biomarker Committee to release the “2022 Consensus on NGS clinical report interpretation”



Pharma service pipeline growth continues at rapid pace

Newly contracted pharma projects

Contract value of new projects entered (RMB millions)





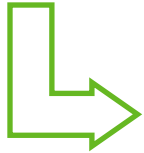
Early detection

Product development since 2016

Demonstrated high specificity and tissue-of-origin detection capability

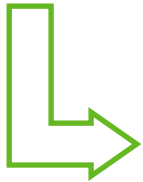
Proof-of-concept
2016 – 2019

- Proof of concept on our methylation based, machine learning aided technology platform
- Results published on *Nature Biomedical Engineering*, “Ultrasensitive detection of circulating tumour DNA via deep methylation sequencing aided by machine learning”



3-cancer
2017 – 2020

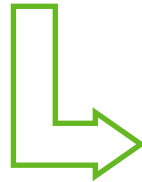
- Lung, Colorectal Cancer (CRC), Hepatocellular Carcinoma (HCC)
- Results released at AACR Special Conference on Liquid Biopsy, Jan 2020
- 95.1% specificity and 80.8% sensitivity¹



Product development complete. Entering commercialization 2022

6-cancer
2018 – Nov 2020

- Lung, CRC, HCC, Ovarian, Pancreatic, Esophageal
- Results released at ESMO Asia, Nov 2020
- 98.3% specificity and 80.6% sensitivity²
- Tissue-of-origin (TOO) result in 98.6% cases; accuracy 81.0%²



Product development in progress

9-cancer
2019 – Ongoing

- Additional cancer types: Gastric, Biliary Tract, Head & Neck
- PROMISE study and PREDICT study

22-cancer³
2020 – Ongoing

- BR-22 covers 88% of China’s cancer incidence
- Ongoing PRESCIENT study

Notes:

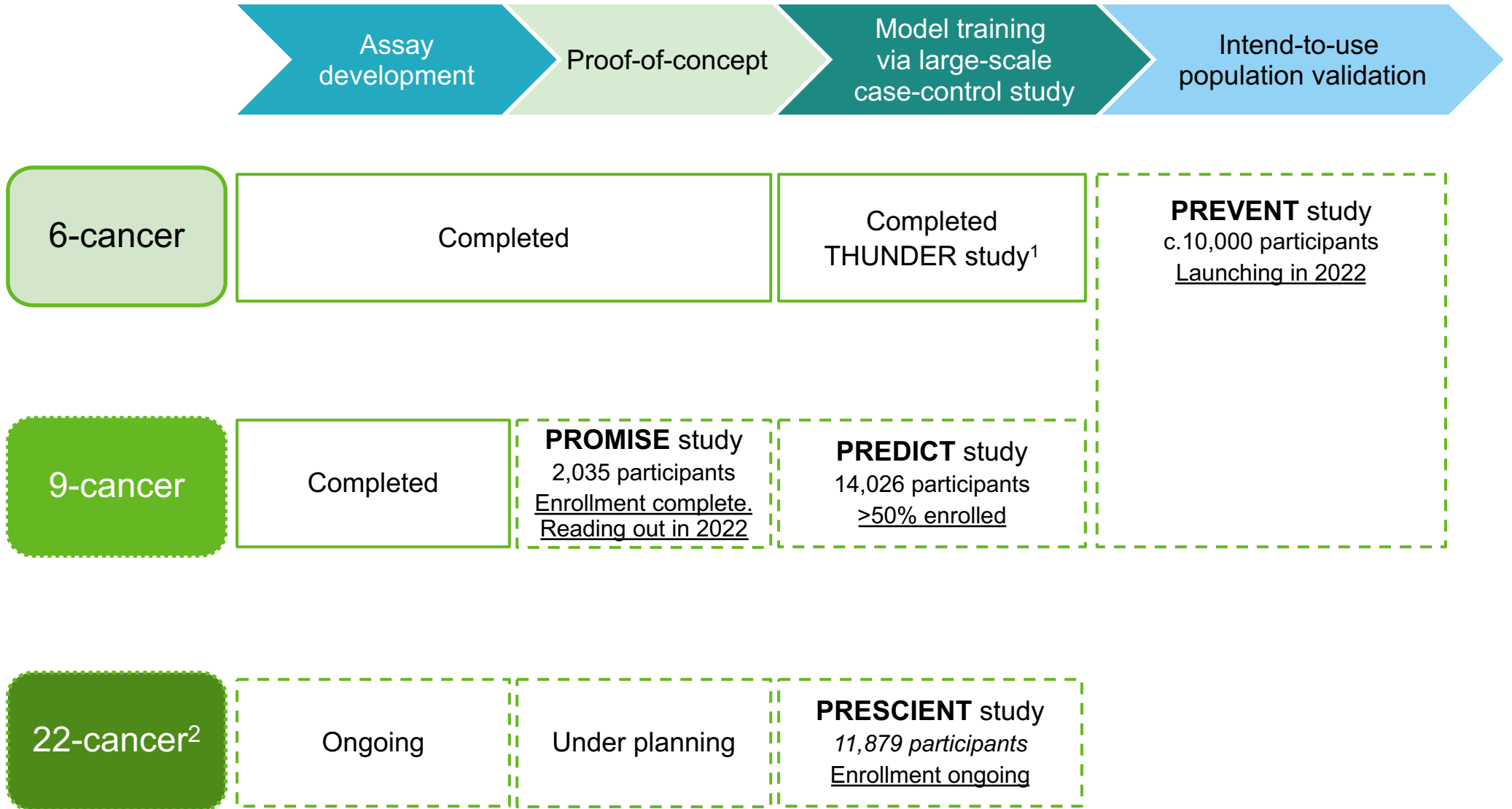
¹ Training and validation cohorts combined, 490 cancer samples, 226 control samples. Sample size is aggregated through a series of case-control studies. 95.1% specificity (95% CI 91.2-97.4) and 80.8% sensitivity (95% CI 77.0-84.1)

² Validation cohort, 351 cancer samples, 288 control samples. Sample size is aggregated through a series of case-control studies. 98.3% specificity (95% CI 95.8-99.4) and 80.6% sensitivity (95% CI 76.0-84.6). Further details in Appendix 1.

³ Final number of cancer types subject to development progress

Clinical programs

9-cancer first read-out expected in 2022. PROMISE study enrollment and analysis completed



Notes:

¹ THUNDER series of studies. Latest results presented at ESMO Asia, Nov 2020

² Final number of cancer types subject to development progress

Burning Rock's early detection technology

Globally competitive technology with multi-cancer validation

Competitive technology

Methylation + machine learning to overcome challenges of low ctDNA abundance and TOO, leading to feasibility for multi-cancer early detection

Multi-cancer validation data

nature
biomedical engineering

ARTICLES

<https://doi.org/10.1038/s41551-021-00746-5>



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

VIRTUAL
2020 ESMO ASIA

Early detection and localization of multiple cancers using a blood-based methylation assay (ELSA-seq)



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

ASCO 2022

Clinical validation of a multicancer detection blood test by circulating cell-free DNA (cfDNA) methylation sequencing: The THUNDER study.

Data read-out on analytical performance of ELSA-seq

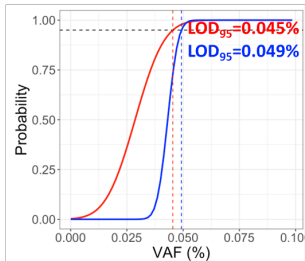
← AACR Annual Meeting 2022 Itinerary Planner Home

Session OPO.CL11.01 - Biomarkers

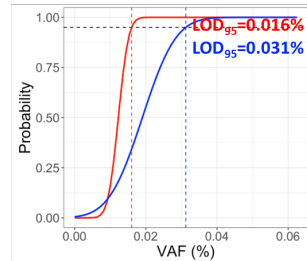
5116 - Analytical performance of ELSA-seq, a blood-based test for early detection of multiple cancers

- **Analytical sensitivity.** The limit of detection with 95% probability (LOD_{95}) was established using 5ng DNA, the lowest claimed input amounts. Two models were assessed with a fixed training specificity at 95% (MCDBT-1) and 99% (MCDBT-2), respectively. Among six tested cancer types, the LOD_{95} was estimated down to 0.02% with respect to VAF.

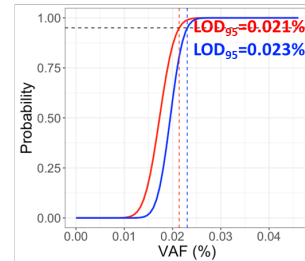
Lung cancer (EGFR:p.L858R)



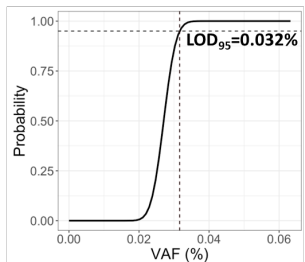
Colorectal cancer (EGFR:p.G719S)



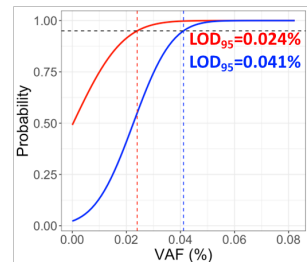
Liver cancer (NRAS:p.Q61L)



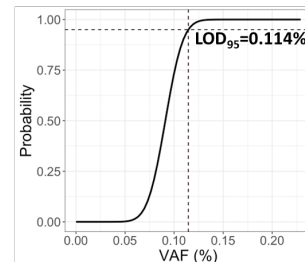
Ovarian cancer (EGFR:p.R215Q)



Esophageal cancer (TP53:p.H214R)



Pancreatic cancer (KRAS:p.G12R)



Full analytical validation study was conducted on ELSA-seq. LoD was demonstrated to be between 0.02% and 0.11% across different cancer types.

Figure 3: The LOD_{95} for 6 cancer types using two prediction models. Probit fit of DOC accuracy versus VAF using cell line dilution series. The red and blue curves represent MCDBT-1 and MCDBT-2 results, respectively. The black curves indicate the same results obtained by both models. The dotted lines indicate the LOD_{95} for each model.

Leadership in multi-cancer early detection

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

Challenges

BNR position

1

Technology

Low amount of cancer signal
in the circulating bloodstream, much more
challenging vs. 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 with studies over 10,000+ subject scale launched

3

Regulatory

First-in-class in nature
with no established regulatory pathway

Leading regulatory capability in China

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

4

Commercial

Unprecedented product

Multi-pronged approach

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

Leadership from top-tier principal investigators key to clinical success

Also drives increasing recognition on multi-cancer early detection among clinicians

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 basis¹
 - Ranked top 5 in the 2019 China's general hospital rankings²
- Other sites include but not limited to
 - Ruijin Hospital
 - Shanghai Jiaotong University School of Medicine
 - Fudan University Shanghai Cancer Center

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 Sciences³
 - 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
- Other sites include but not limited to
 - Beijing Cancer Hospital
 - Jilin Cancer Hospital
 - Hubei General Hospital

Principal Investigators

Prof. Jie He



Prof. Jie Wang



Head of the Dept. of Medicine, CHCAMS

- Fellow of the Chinese Academy of Sciences
- President of CHCAMS

Notes:

¹ Based on 2018 statistics

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

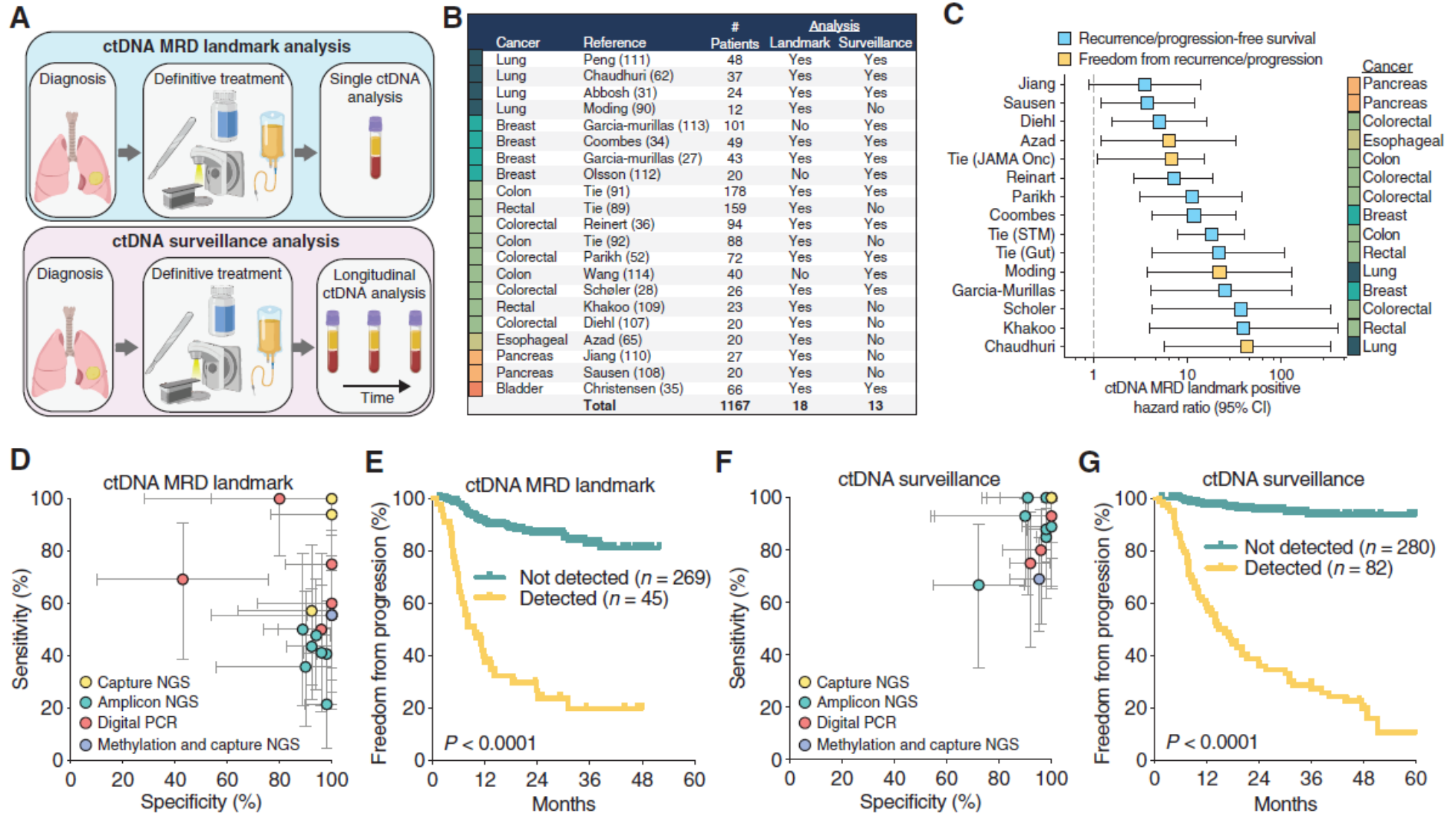
³ CHCAMS



MRD

Clinical utilities of MRD in solid tumors

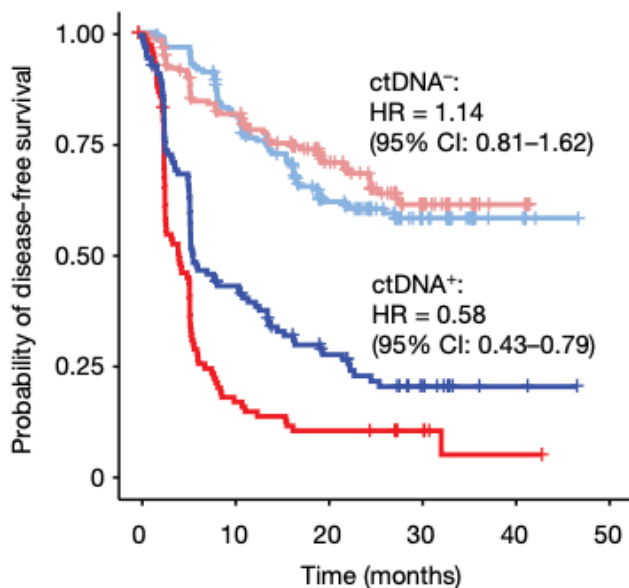
1) risk stratification and regimen selection (landmark analysis), 2) relapse monitoring (surveillance analysis)



Clinical utilities of MRD in solid tumors

1) risk stratification and regimen selection (landmark analysis), 2) relapse monitoring (surveillance analysis)

IMvigor010 – MRD demonstrating CDx potential



No. at risk		Time (months)					
		0	10	20	30	40	50
— Atezolizumab	ctDNA ⁻	184	144	85	44	5	0
		183	140	90	46	6	0
— Atezolizumab	ctDNA ⁺	116	48	25	13	2	0
		98	17	10	5	1	0

Nature. 2021 Jun 16. doi: 10.1038/s41586-021-03642-9.

Chinese oncologists developing consensus on MRD applications in solid tumors, e.g. lung cancer

第18届中国肺癌高峰论坛
——肺癌分子(微小)残留病灶(MRD)的检测和临床应用共识

共识一：MRD的概念

- 肺癌分子残留病变，指的是经过治疗后，传统影像学(包括PET/CT)或实验室方法不能发现，但通过液体活检发现的癌来源分子异常，代表着肺癌的持续存在和临床进展可能；
- 肺癌分子异常：指的是在外周血可稳定检测出丰度 $\geq 0.02\%$ 的ctDNA，包括肺癌驱动基因或其他的 I / II 类基因变异。

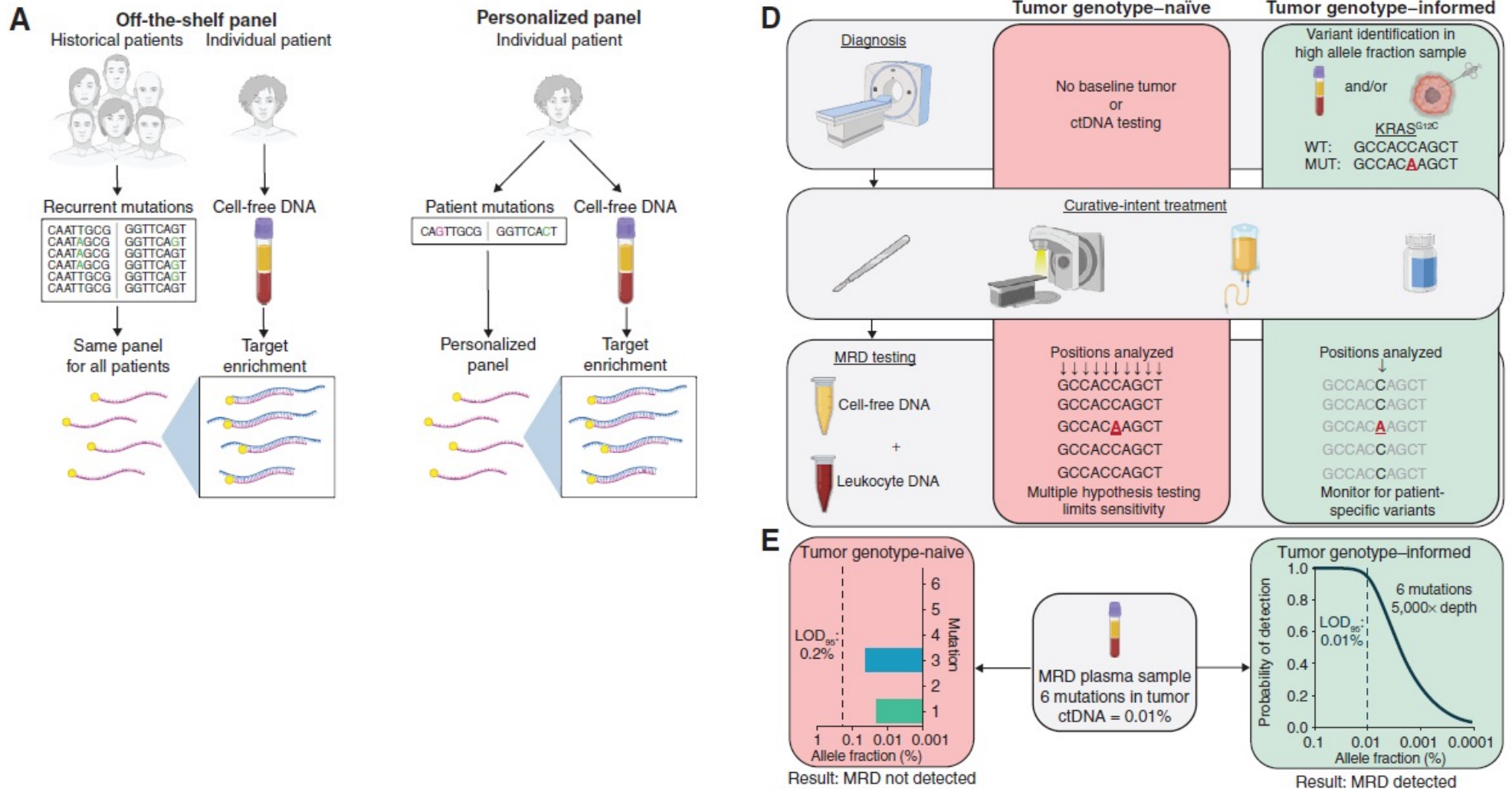
共识二：MRD检测的基本技术要求

- MRD检测的基本技术，包括Tumor-informed assays(个体化定制)和 Tumor agnostic assays(NGS panel和多组学技术)，目前均处在探索阶段，需要前瞻性研究确定其敏感性、特异性和预测价值；
- 采用二代测序技术(NGS)，所选的多基因 panel中必须覆盖患者 I / II 类基因变异，基本技术标准是可稳定检出丰度 $\geq 0.02\%$ 的ctDNA；
- 驱动基因阳性的非小细胞肺癌，MRD的分子panel应包括该驱动基因；
- MRD评估报告中必须包括cfDNA丰度， ctDNA丰度，所检测基因VAF值；
- 需要建立针对免疫治疗的MRD标准。

Chinese lung cancer consensus on MRD detection and clinical application, 2021

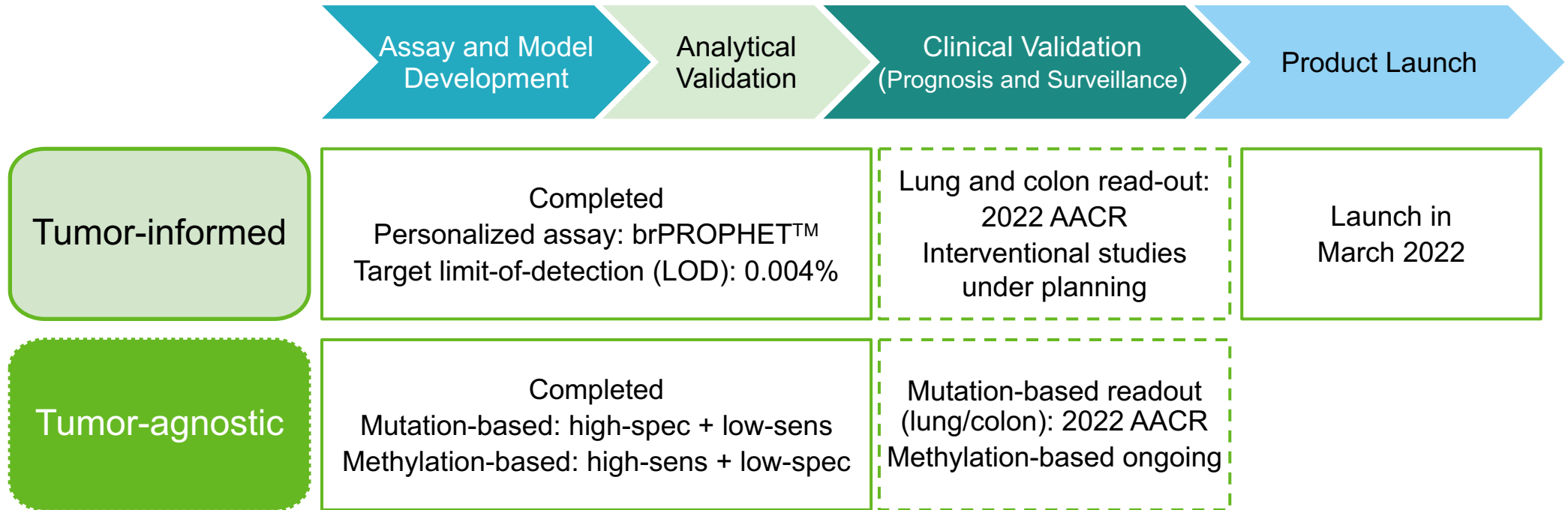
Clinical utilities of MRD in solid tumors

Fixed panel vs. personalized panel approaches



MRD product pipelines

Personalized approach (brPROPHET™) demonstrating stronger performance, esp. in early stage patients



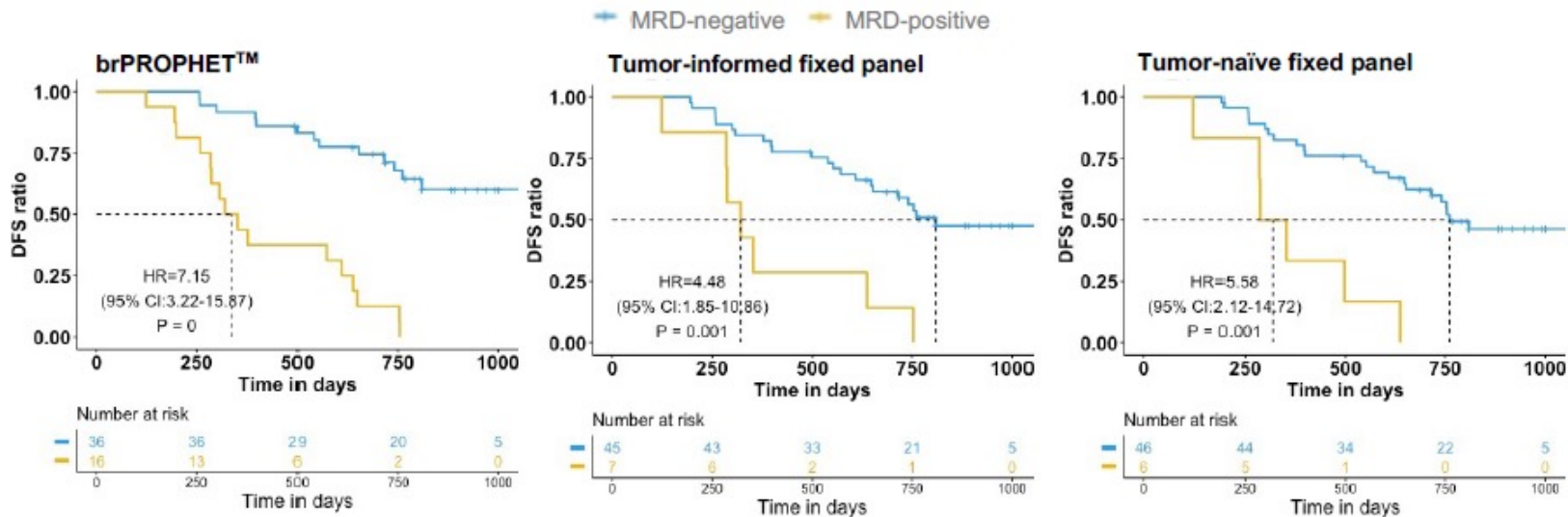
Recent trends on MRD clinical adoption in China

- MRD recommended for relapse-risk prediction for early-stage NSCLC patients by the 2021 *Chinese Lung Cancer Clinician Consensus*
- MRD technology is required to demonstrate an LOD lower than 0.02%
- Some clinicians and pharma companies are exploring MRD-driven patient-selection or treatment-plus/minus adjuvant therapy studies
- Most NGS companies only offer mutation panel-based liquid biopsy assays, with sub-optimal sensitivity for MRD utility

MRD clinical validation data readout NSCLC

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

5916 - Tumor-informed patient-specific panel outperforms tumor-naïve and tumor-informed fixed panel for circulating tumor DNA (ctDNA)-based postoperative monitoring of non-small cell lung cancer (NSCLC)



Three-year prognostication with brPROPHET™ assay at B+C time-points yielded higher sensitivity (59% vs 26% vs 22%), negative predictive value (66% vs 51% vs 50%), and hazard ratio (7.15, 95%CI [3.2-15.9] vs 4.48 [1.9-10.9] vs 5.58 [2.1-14.7]) as compared with tumor-informed and tumor-naïve fixed panel assays.

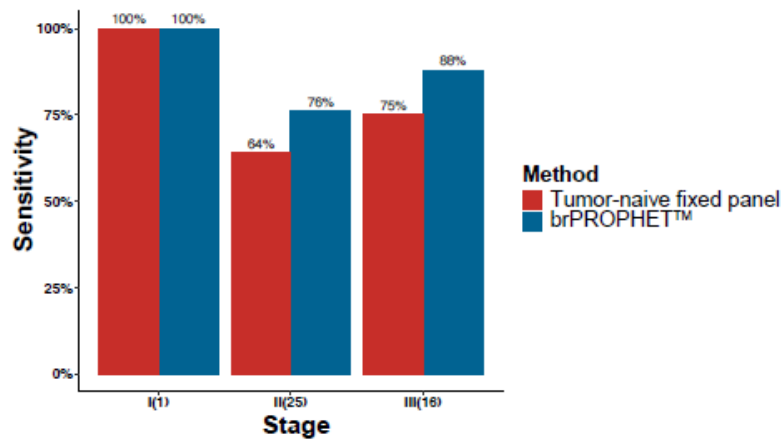
In the full MEDAL cohort, MRD- patients assessed by brPROPHET™ achieved a 12-month recurrence-free rate > 95% (unpublished data)

MRD clinical validation data readout

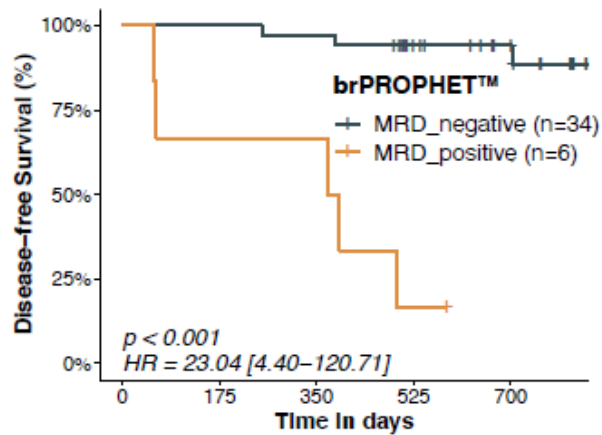
CRC

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)

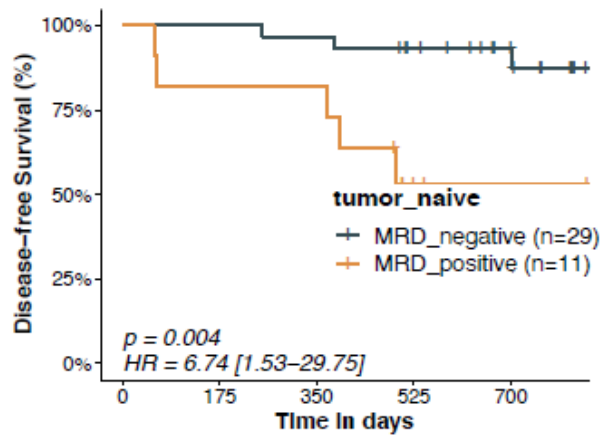


brPROPHET™ demonstrated superior sensitivity and specificity to fixed panel in pre-operative ctDNA detection and post-operative MRD calling among relapsed patients



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

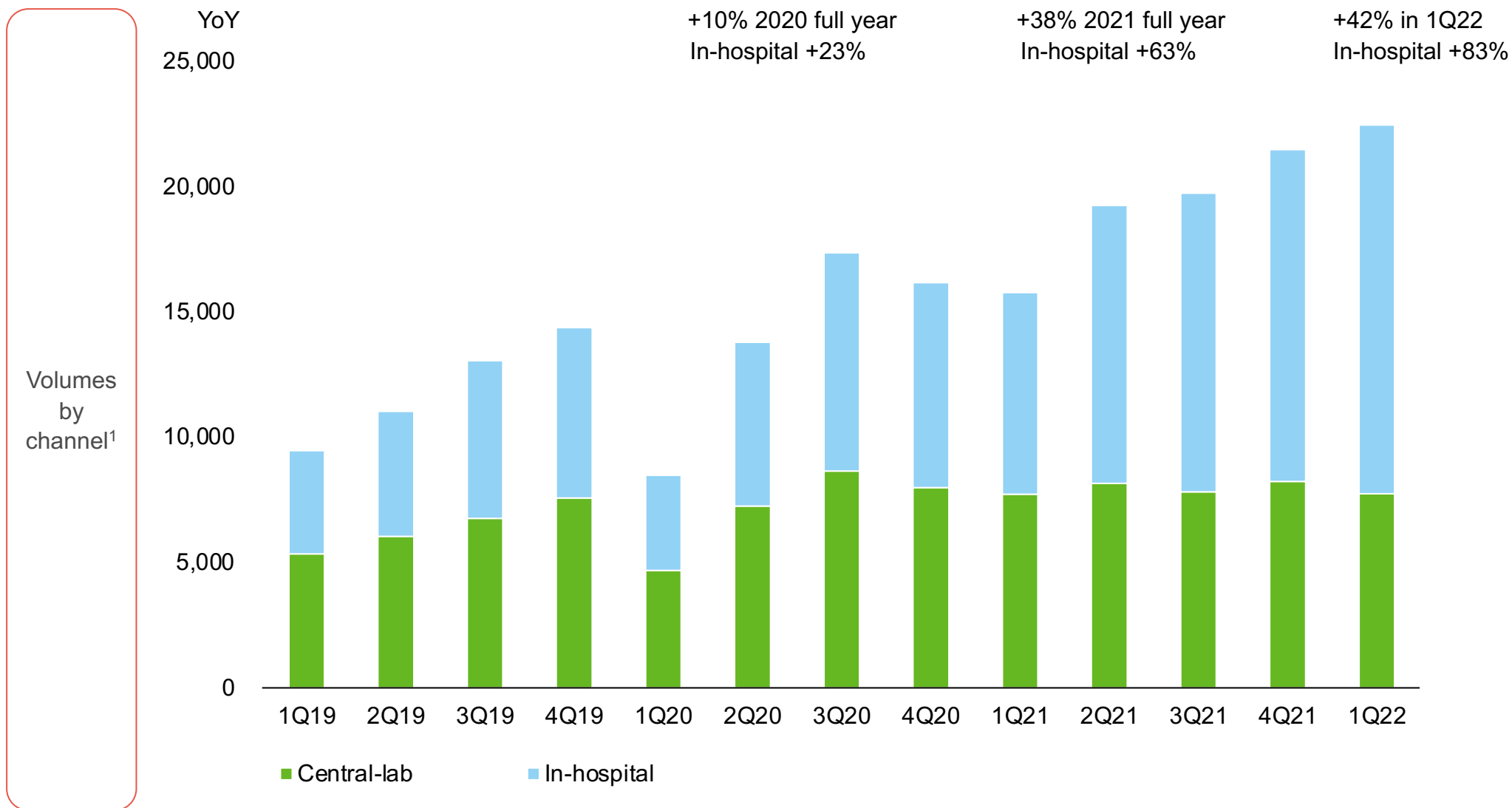


Financials

Continued in-hospital strength and new products driving growth uplift

1Q22 growth trended up, +42% YoY (vs. +33% YoY in 4Q21) despite Covid challenges

Central-lab volume growth turned positive, driven by new product ramp-up



Notes:

¹ Central-lab (LDT) volumes represented by the number of patients tested. In-hospital (IVD) volumes represented by the number of testing kits shipped to partner hospitals

Latest trends

Positive growth in Apr despite Covid challenges (Shanghai close to stand-still, worse than during 2020)
 Covid dynamics fluid in China, with Shanghai looking to re-open

Volume growth YoY ¹	Jan 22	Feb Chinese new year	Mar	Apr
All regions	+74%	+51%	+17%	+15%
Central-lab	+9%	+14%	-4%	-21%
In-hospital	+149%	+95%	+36%	+60%
Ex. Shanghai	+54%	+48%	+25%	+37%
Central-lab	+9%	+13%	+1%	-13%
In-hospital	+108%	+106%	+52%	+108%

Notes:

¹ Central-lab (LDT) volumes represented by the number of patients tested. In-hospital (IVD) volumes represented by the number of testing kits shipped to partner hospitals

Financials

1Q22 revenue growth (+27%) above full-year guide (+22%), opex declined sequentially
RMB1.3bn / US\$211m cash and short-term investment on balance

RMB millions	2021	19 YoY	20 YoY	21 YoY	1Q21	2Q21	3Q21	4Q21	1Q22	1Q22 YoY	1Q22 QoQ	2022 Guide
Revenue	507.9	83%	13%	18%	106.6	127.3	126.6	147.3	135.5	27%	(8%)	620
Central lab	319.4	71%	8%	7%	74.6	80.0	78.8	86.0	74.2	(1%)	(14%)	
In-hospital ¹	165.1	164%	34%	40%	29.0	40.5	43.7	51.9	49.0	69%	(6%)	
Pharma	23.4	25%	(17%)	59%	3.1	6.8	4.1	9.4	12.3	297%	31%	
Gross profit	364.1	102%	15%	16%	76.9	90.2	91.6	105.4	87.6	14%	(17%)	
Total opex	1,161.2	49%	64%	60%	248.8	292.3	262.7	357.5	350.4	41%	(2%)	
R&D ²	338.2	43%	45%	57%	55.0	87.2	79.2	116.7	107.2	95%	(8%)	
S&M ²	293.6	49%	9%	75%	52.5	65.2	74.7	101.1	87.4	66%	(14%)	
G&A ²	248.6	40%	44%	39%	56.9	56.8	55.5	79.5	76.0	34%	(4%)	
SBC ³	280.8				84.4	83.0	53.3	60.2	79.8			
Operating profit	(797.1)				(171.9)	(202.0)	(171.1)	(252.1)	(262.8)			
GP margin	71.7%				72.2%	70.9%	72.3%	71.5%	64.6%			
Non-GAAP GP margin ⁴	72.5%				72.4%	71.2%	73.4%	72.9%	68.4%			
Opex ² / revenue	173%				154%	164%	165%	202%	200%			
S&M ² / revenue	58%				49%	51%	59%	69%	65%			

Notes:

¹ 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

² Excluding share based compensation (SBC)

³ Share based compensation

⁴ Non-GAAP gross margin, which is defined as gross margin excluding depreciation and amortization

Appendix 1

Early detection

ESMO Asia mini-oral presentation, Nov 2020

Overview of training and validation sets

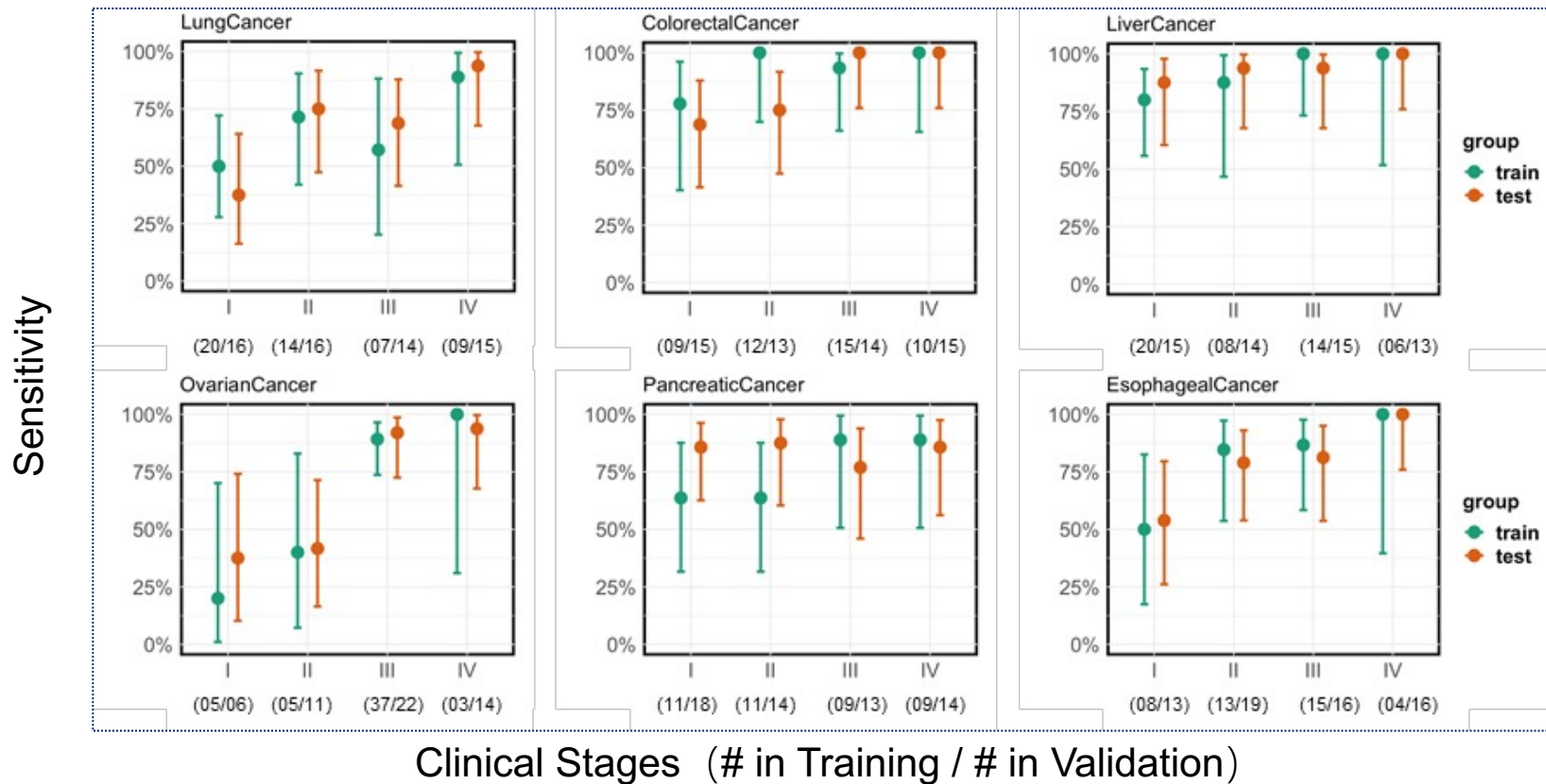
Training	Control	Cancer	LC	CRC	LIHC	OVCA	PAAD	ESCA
total	195	274	50	46	48	50	40	40
age, mean+/-SD	53+/-6	57+/-8	60+/-6	60+/-8	55+/-8	50+/-8	59+/-7	57+/-6
age, min/max	40/72	40/75	47/74	44/75	43/72	40/73	42/71	45/70
sex, female, n (%)	128 (70)	110 (40)	16 (32)	21 (46)	4 (8)	50 (100)	14 (35)	5 (13)
clinical stage, n (%)								
I		73 (27)	20 (40)	9 (20)	20 (41)	5 (10)	11 (27)	8 (20)
II		63 (23)	14 (28)	12 (26)	8 (17)	5 (10)	11 (27)	13 (33)
III		97 (35)	7 (14)	15 (32)	14 (29)	37 (74)	9 (23)	15 (37)
IV		41 (15)	9 (18)	10 (22)	6 (13)	3 (6)	9 (23)	4 (10)

Validation	Control	Cancer	LC	CRC	LIHC	OVCA	PAAD	ESCA
total	288	351	61	57	57	53	59	64
age, mean+/-SD	54+/-6	59+/-8	62+/-7	61+/-9	54+/-8	54+/-7	61+/-9	62+/-6
age, min/max	40/74	40/75	45/74	44/75	40/73	42/68	40/74	46/74
sex, female, n (%)	171 (59)	146 (42)	22 (36)	21 (37)	9 (16)	53 (100)	19 (32)	22 (34)
clinical stage, n (%)								
I		83 (23)	16 (26)	15 (26)	15 (26)	6 (11)	18 (30)	13 (20)
II		87 (25)	16 (26)	13 (23)	14 (25)	11 (21)	14 (24)	19 (30)
III		94 (27)	14 (23)	14 (25)	15 (26)	22 (42)	13 (22)	16 (25)
IV		87 (25)	15 (25)	15 (26)	13 (23)	14 (26)	14 (24)	16 (25)

1. Similar age distribution between cases and controls, and between training set and validation set
2. Balanced sample size among different stages and cancer types

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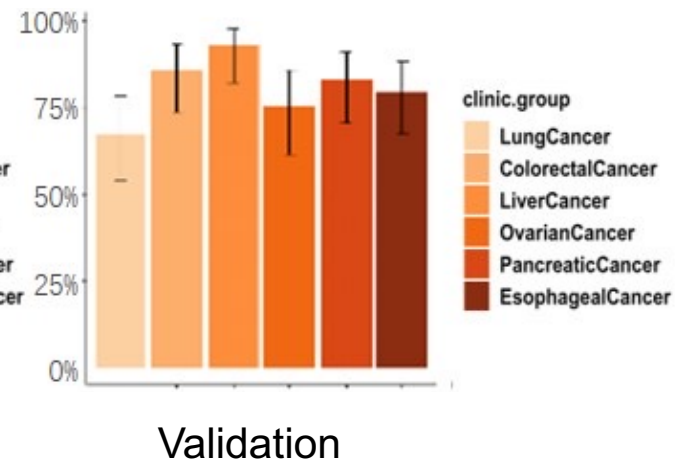
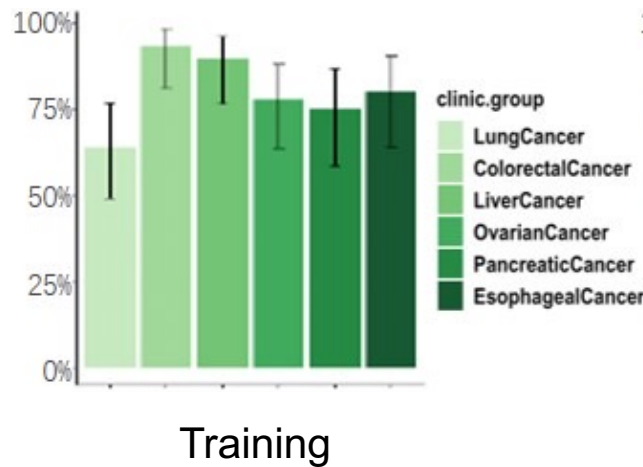
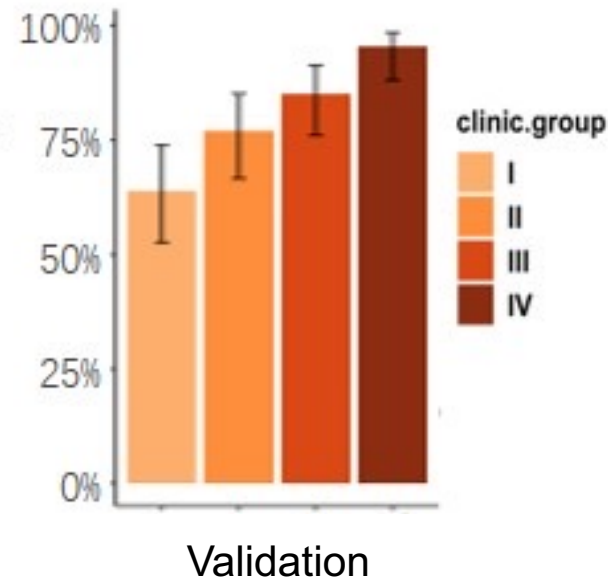
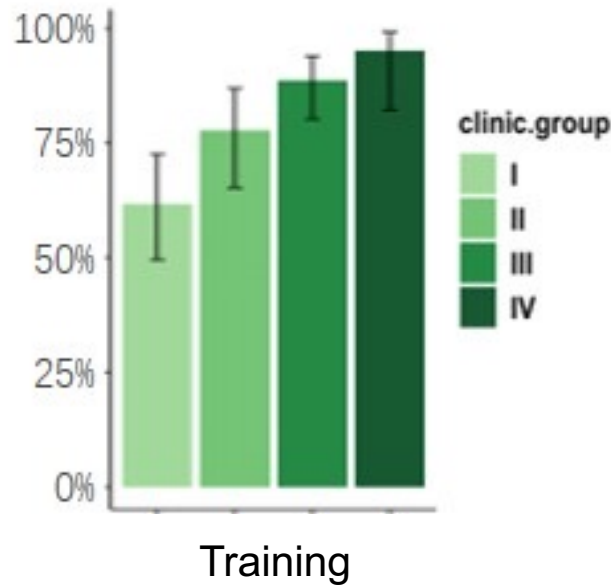
Our test detects cancers at an early stage with high specificity and high sensitivity



- The specificity was **99.5%** (95%CI: 96.7-100%; training) and **98.3%** (95%CI: 95.8-99.4%; validation)
- The sensitivity was **79.9%** (95%CI: 74.6-84.4%; training) and **80.6%** (95%CI: 76.0-84.4%; validation)

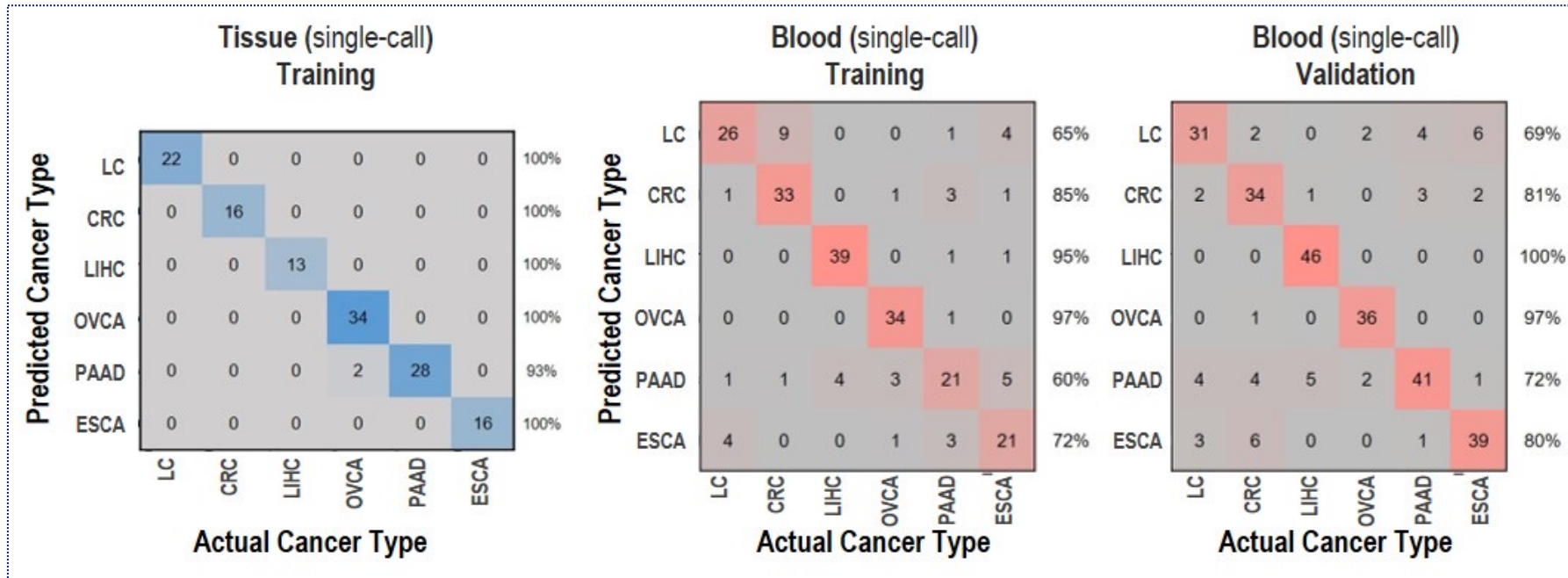
ESMO Asia mini-oral presentation, Nov 2020

Our test detects cancers at an early stage with high specificity and high sensitivity



ESMO Asia mini-oral presentation, Nov 2020

Our test predicts the tissue of origin with high accuracy



- The classifier was able to distinguish different cancer tissue samples with exceptional accuracy (**129/131**).
- **98.6%** of detected cancer blood samples were assigned an organ-source in both training and validation sets:
 - For single organ calls, the predictive accuracy was **79%** (training) and **82%** (validation);
 - For top-two organ calls, the predictive accuracy was **89%** (training) and **87%** (validation).

ESMO Asia mini-oral presentation, Nov 2020

6-cancer test sensitivity by cancer type and stage

Sensitivity and Specificity - Correct#/Total# (%)

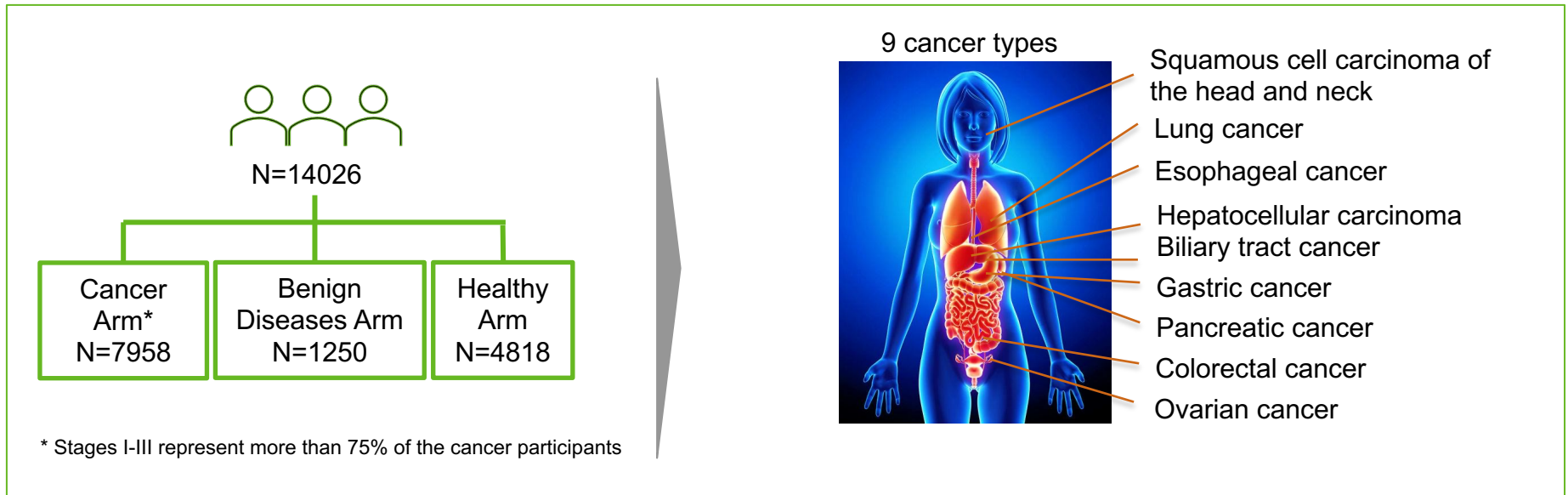
Cancer	Group	I	II	III	IV	Overall
Lung	Train	10/20 (50.0)	10/14 (71.4)	4/7 (57.1)	8/9 (88.9)	32/50 (64.0)
	Test	6/16 (37.5)	12/16 (75.0)	9/14 (64.3)	14/15 (93.3)	41/61 (67.2)
Colorectal	Train	7/9 (77.8)	12/12 (100.0)	14/15 (93.3)	10/10 (100.0)	43/46 (93.5)
	Test	10/15 (66.7)	10/13 (76.9)	14/14 (100.0)	15/15 (100.0)	49/57 (86.0)
Liver	Train	16/20 (80.0)	7/8 (87.5)	14/14 (100.0)	6/6 (100.0)	43/48 (89.6)
	Test	13/15 (86.7)	13/14 (92.9)	14/15 (93.3)	13/13 (100.0)	53/57 (93.0)
Ovarian	Train	1/5 (20.0)	2/5 (40.0)	33/37 (89.2)	3/3 (100.0)	39/50 (78.0)
	Test	2/6 (33.3)	5/11 (45.5)	20/22 (90.9)	13/14 (92.9)	40/53 (75.5)
Pancreatic	Train	7/11 (63.6)	7/11 (63.6)	8/9 (88.9)	8/9 (88.9)	30/40 (75.0)
	Test	15/18 (83.3)	12/14 (85.7)	10/13 (76.9)	12/14 (85.7)	49/59 (83.1)
Esophageal	Train	4/8 (50.0)	11/13 (84.6)	13/15 (86.7)	4/4 (100.0)	32/40 (80.0)
	Test	7/13 (53.8)	15/19 (78.9)	13/16 (81.3)	16/16 (100.0)	51/64 (79.7)
Sensitivity	Train					219/274 (79.9)
	Test					283/351 (80.6)
Specificity	Train					194/195 (99.5)
	Test					283/288 (98.3)

The PREDICT study (NCT04817306)

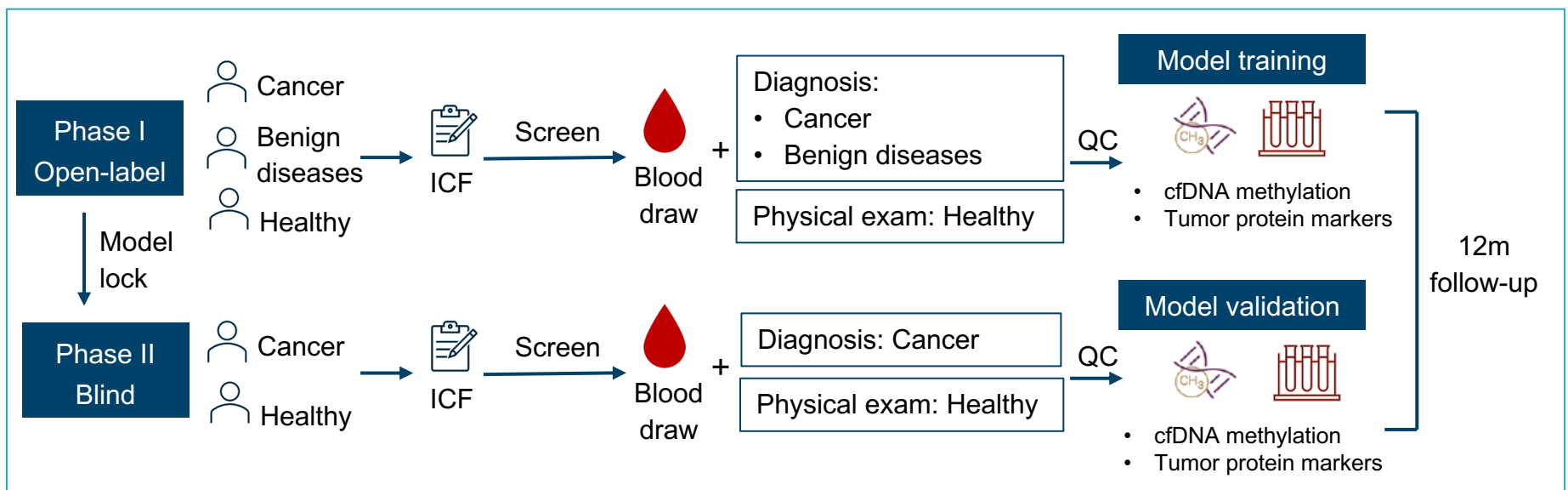
Study design

PREDICT is a *prospective, multi-center, case-control, observational* study for the detection of 9 cancer types through a cell-free DNA (cfDNA) methylation based, machine learning aided model

Participants



Study Design



The PREDICT study (NCT04817306)

Objectives and timeline

Objectives

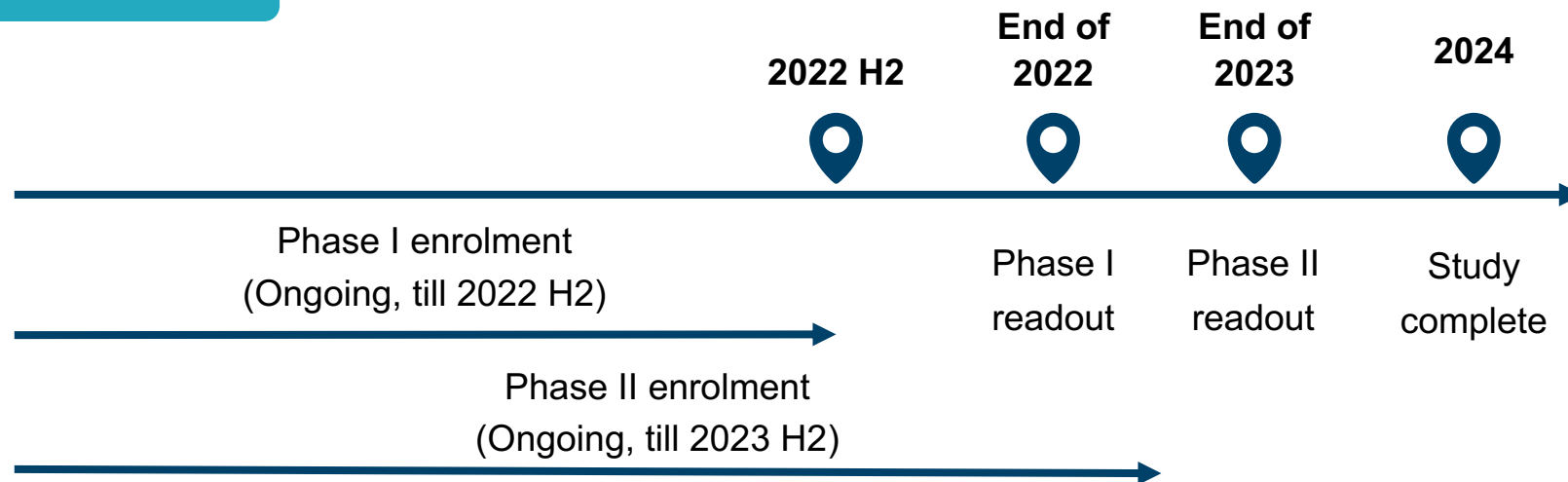
Primary objective:

- To train and validate the *sensitivity, specificity and TOO accuracy* of a cfDNA methylation-based model for early detection of 9 types of cancers

Key secondary objectives:

- To evaluate the sensitivity, specificity and TOO accuracy of a cfDNA methylation-based model in various *types and stages of cancers*
- To evaluate the sensitivity, specificity and TOO accuracy of a cfDNA methylation-based model *combined with other biomarkers*
- To evaluate the *positive predictive value* of a cfDNA methylation-based model among asymptomatic “cancer-free” individuals within a 12-month follow up period

Timeline



The PREDICT study (NCT04817306)

National Oncology Conference on Standardized Diagnosis and Treatment, Beijing, 14th-16th May 2021

国内率先启动“泛癌种”早筛研究

cfDNA甲基化

多癌种

基于cfDNA甲基化检测的早期癌症鉴别诊断模型在多癌种中的探索及验证：一项前瞻性、多中心研究 (Pan-Cancer Early Detection Project, PREDICT)

研究预计纳入癌症、良性病变及健康受试者；
样本量：14026例

NIH U.S. National Library of Medicine
ClinicalTrials.gov
Pan-cancer Early Detection project (PREDICT)
ClinicalTrials.gov Identifier: NCT04817306
Recruitment Status: Not yet recruiting
First Posted: May 12, 2020
Last Update Posted: May 14, 2020
See Contacts and Locations

10

多癌种

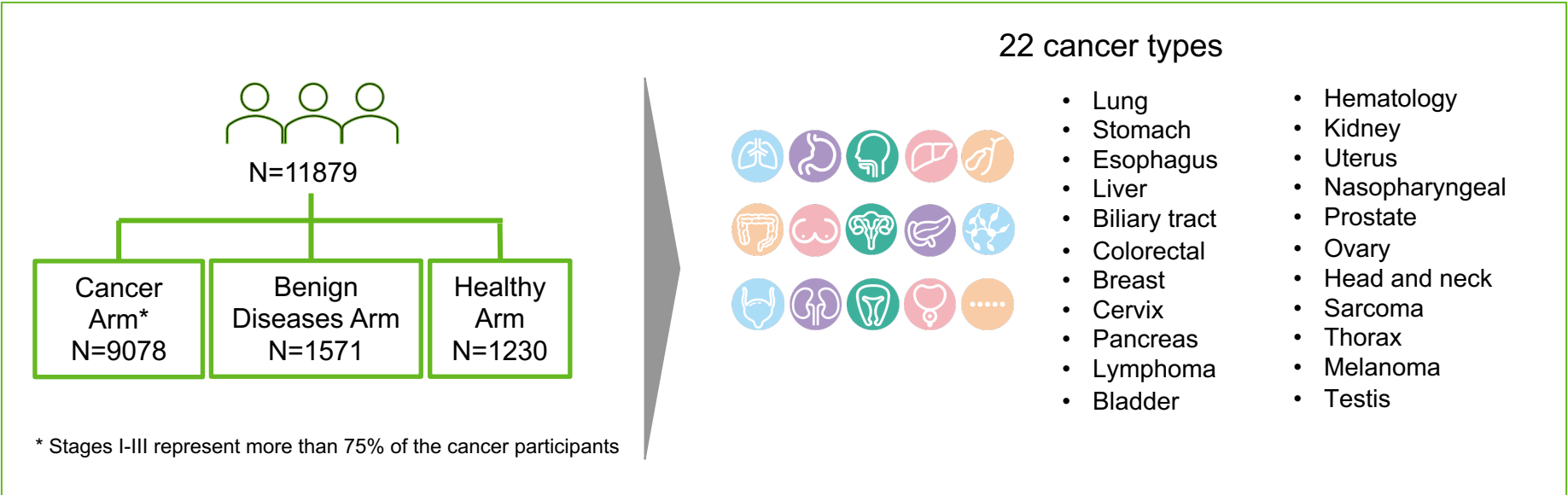
ClinicalTrials.gov
Pan-cancer
ClinicalTrials.gov
Recruitment
First Posted
Last Update
Posted

The PRESCIENT study (NCT04822792)

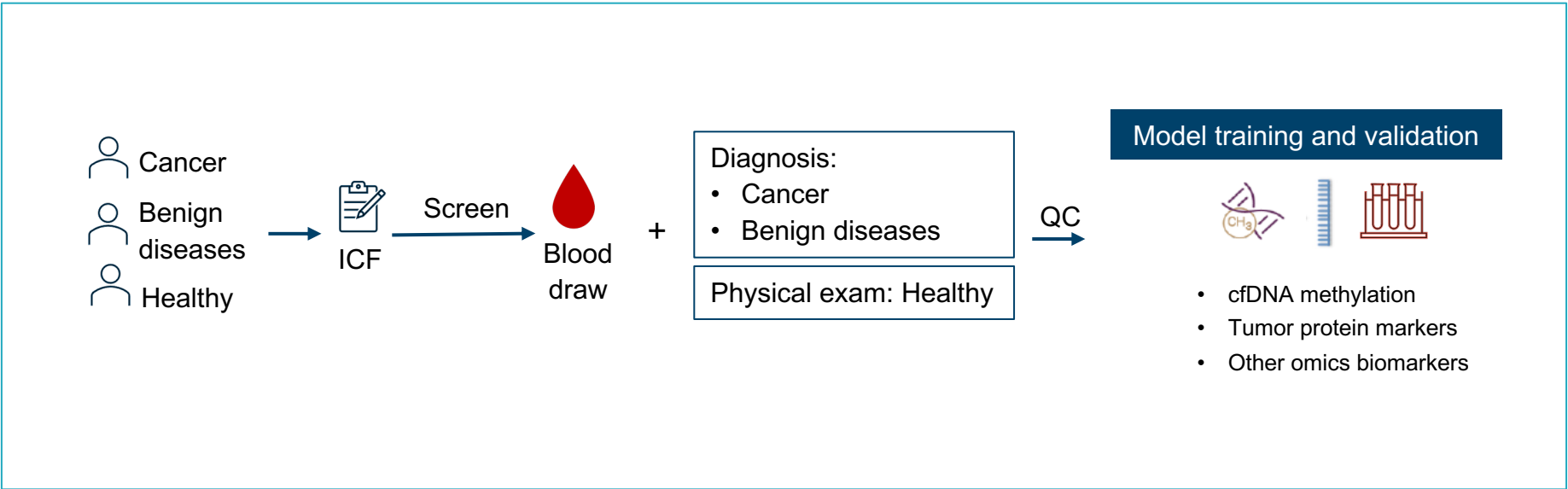
Study design

PRESCIENT is a *prospective, multi-center, case-control, observational* study aimed to train and validate the performance of a multi-omics model in the detection of 22 cancers

Participants



Study Design



The PRESCIENT study (NCT04822792)

Objectives and timeline

Objectives

Primary objective

- To train and validate the *sensitivity, specificity and TOO accuracy* of a cfDNA methylation-based model combined with tumor protein markers for early detection of 22 types of cancers

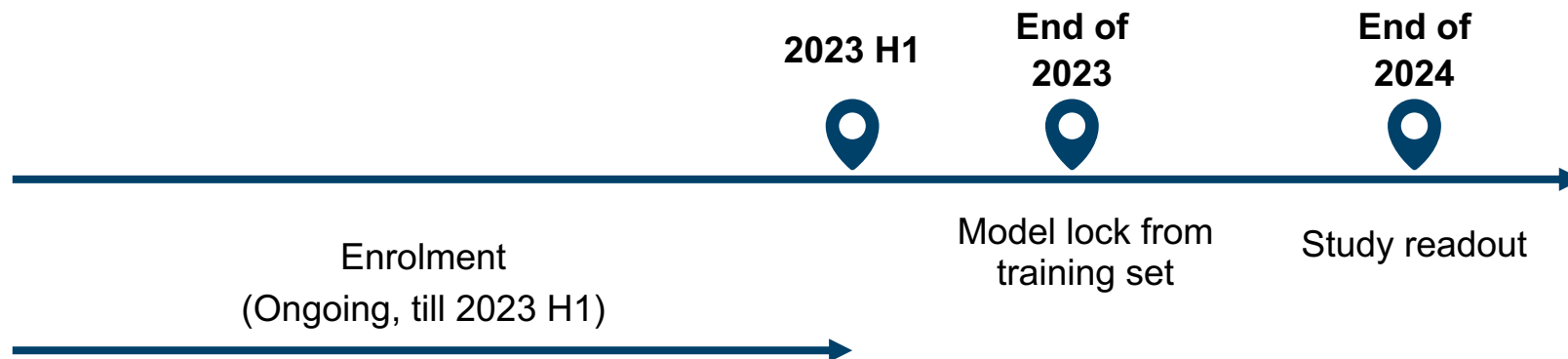
Secondary objective

- To evaluate the sensitivity and specificity of a cfDNA methylation-based model combined with tumor protein markers in early detection of 22 types of cancers *in different stages*

Exploratory objective:

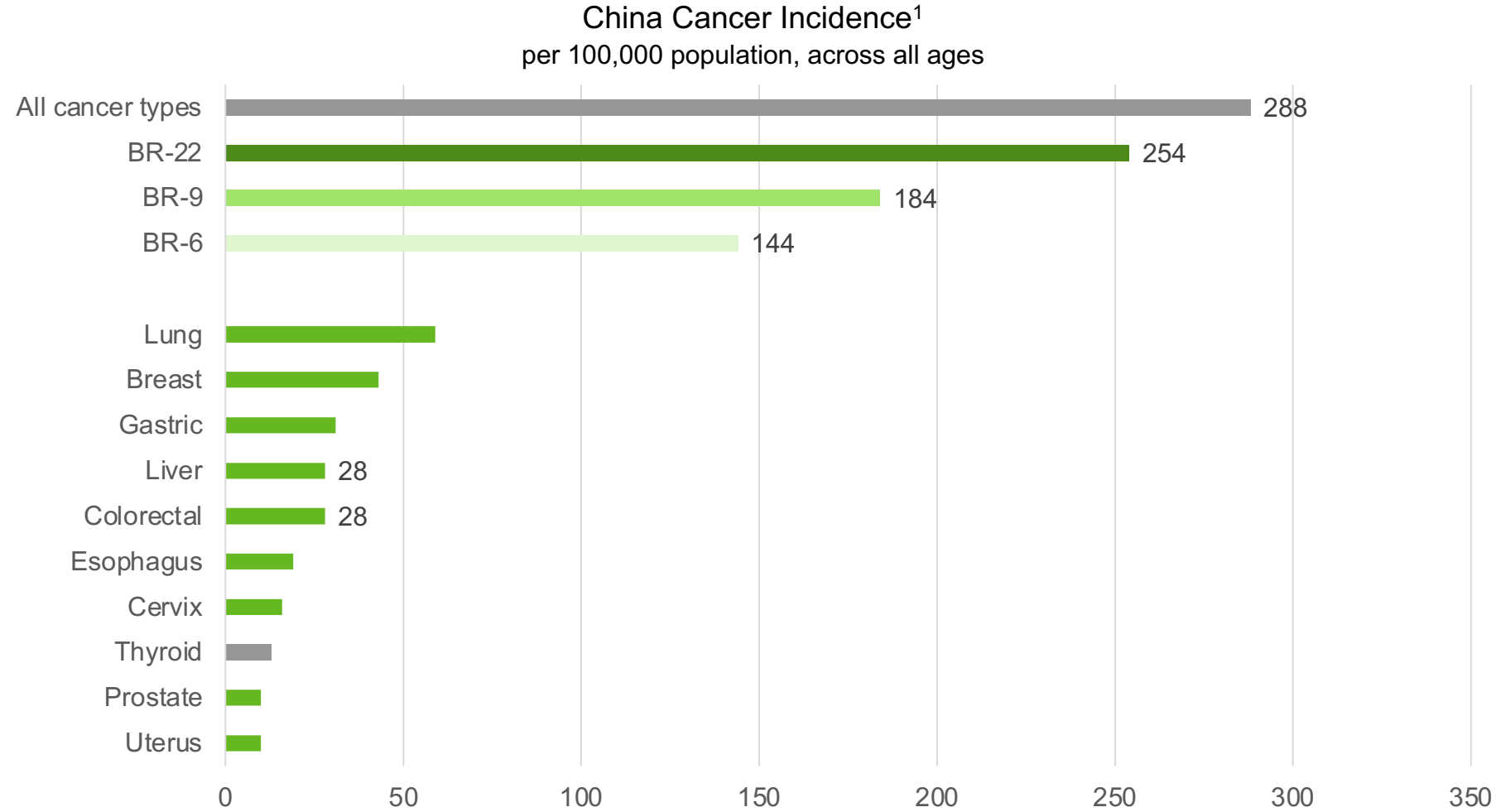
- To evaluate the sensitivity and specificity of *other genetic/epigenetic biomarkers combined with a cfDNA methylation-based model and tumor protein markers* in early detection of cancers

Timeline



Multi vs. single cancer early detection

Multiple times larger TAM



BR-22 covers 88% of China's cancer incidence²

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

Multi vs. single cancer early detection in China

Significantly higher technology barrier

Single-cancer test

- Established technology, typically PCR based, with readily available products
 - US – First FDA approved product in 2014 (first submission in 2012)
 - China – NMPA approved products (class-III, including tissue and blood-based) in 2017, 2018, 2019, 2020, 2021, etc
- Small panel, low cost
- Relatively simple genomic data analytics

Multi-cancer test


- Biologically, blood-based tests are multi-cancer in nature
- Highly complex technology with product risk
 - Globally, only a small number of innovators have locked-down products going under intended-use validation
- Data as a key factor for development and validation
 - Evolving dataset leads to continuous product improvement and greater validation
- Unprecedented commercial potential
 - Possibility to fundamentally shift oncology landscape from late-stage therapeutics to earlier stage intervention

Appendix 2

Therapy selection

NMPA approved NGS panels

NMPA approved testing kit by major NGS-focused companies¹

	First NMPA-approved kit	Second NMPA-approved kit
 燃石医学 Burning Rock Dx	EGFR, ALK, BRAF, KRAS Approved in Jul 2018 <u>First approved NGS kit in China</u>	EGFR, KRAS, MET, ERBB2, BRAF, PIK3CA, ALK, ROS1, RET Approved in Mar 2022
Novogene 诺禾	EGFR, KRAS, BRAF, PIK3CA, ALK, ROS1 Approved in Aug 2018	
Geneseeq 世和	EGFR, ALK, ROS1, BRAF, KRAS, ERBB2 Approved in Sep 2018	
BGI 华大	EGFR, KRAS, ALK Approved in Aug 2019	
Gene+ 吉因加	EGFR, KRAS, ALK Approved in Dec 2019	
Genetron 泛生子	EGFR, KRAS, BRAF, ERBB2, PIK3CA, ALK, ROS1, MET Approved in Feb 2020	
Genecast 臻和	KRAS, NRAS, BRAF, PIK3CA Approved in Mar 2021	
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 CNV² mutation type, with MET exon14 skipping

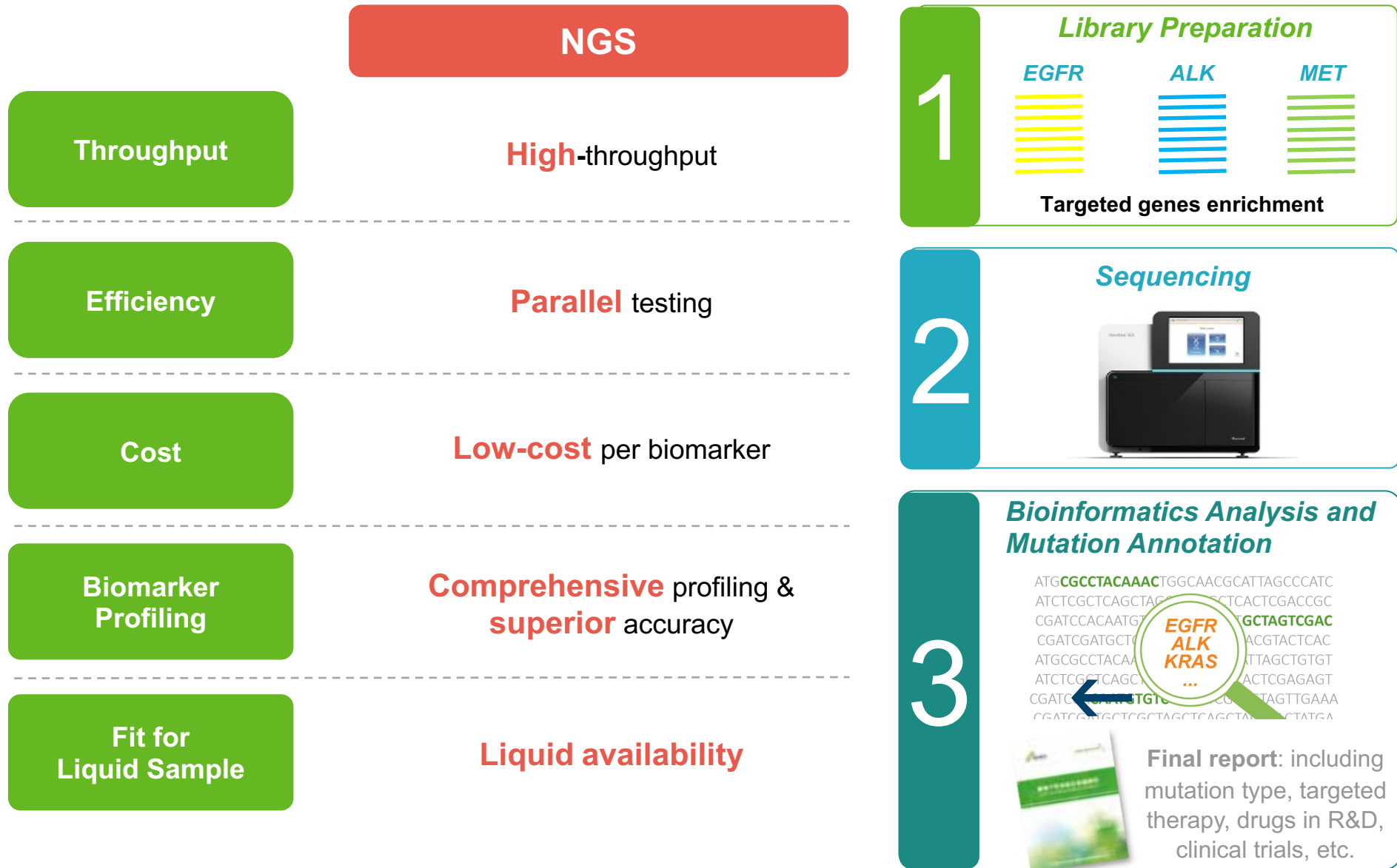
Notes:

¹ Major NGS-focused companies listed. The list is not exhaustive. A total of 13 kits have been approved by the NMPA as of the date of this presentation

² 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

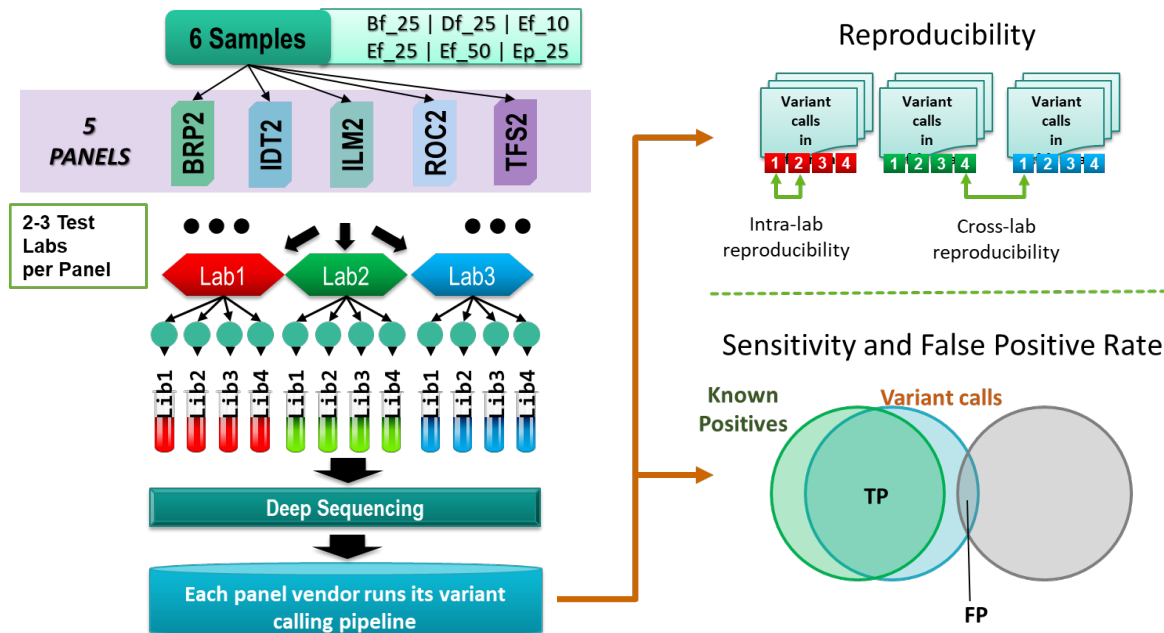
- Enzymatic fragmentation
 - better ligation efficiency
- Gel-based size selection (160bp-180bp) to mimic cfDNA
- 1ng/ul to mimic concentration after DNA extraction from plasma
- Ep: 40ng/ml Ef in synthetic plasma

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

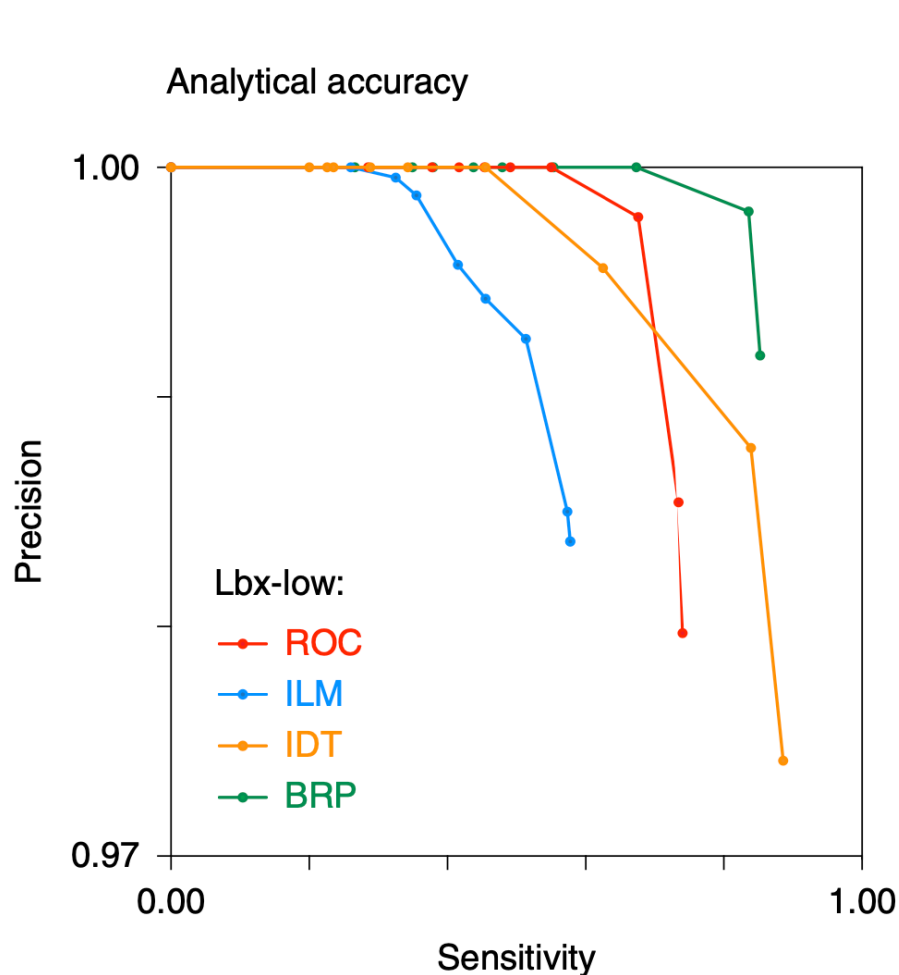
Liquid
Biopsy

Participating assays and study design

Name	Vendor	ctDNA assay	Sequencing platform	Target genes	Reportable region (kb)	Coding (kb)	CTR (kb)	Negatives (× 1,000)	Variants
ROC	Roche Sequencing Solutions	AVENIO ctDNA (Expanded Kit)	Illumina NextSeq	77	161.7	140.2	103.8	47.1	189
ILM	Illumina	TruSight Tumor 170 + UMI	Illumina NovaSeq	154	501.0	390.1	338.4	133.0	574
IDT	Integrated DNA Technologies	xGen Non-small Cell Lung Cancer	Illumina NovaSeq	24	110.1	93.2	76.5	39.3	130
BRP	Burning Rock Biotech	Lung Plasma v4	Illumina NovaSeq	168	226.9	148.5	125.1	53.4	229
TFS	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 ≥ 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.**”