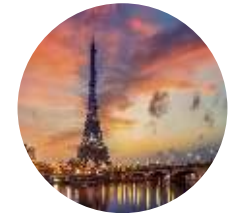# Precision Medicine In Practice For NSCLC

Rania Gaspo, BPharm, PhD

Global Therapy Area Expert / Oncology

Cerba Research
Your precision medicine partner

01

Introduction

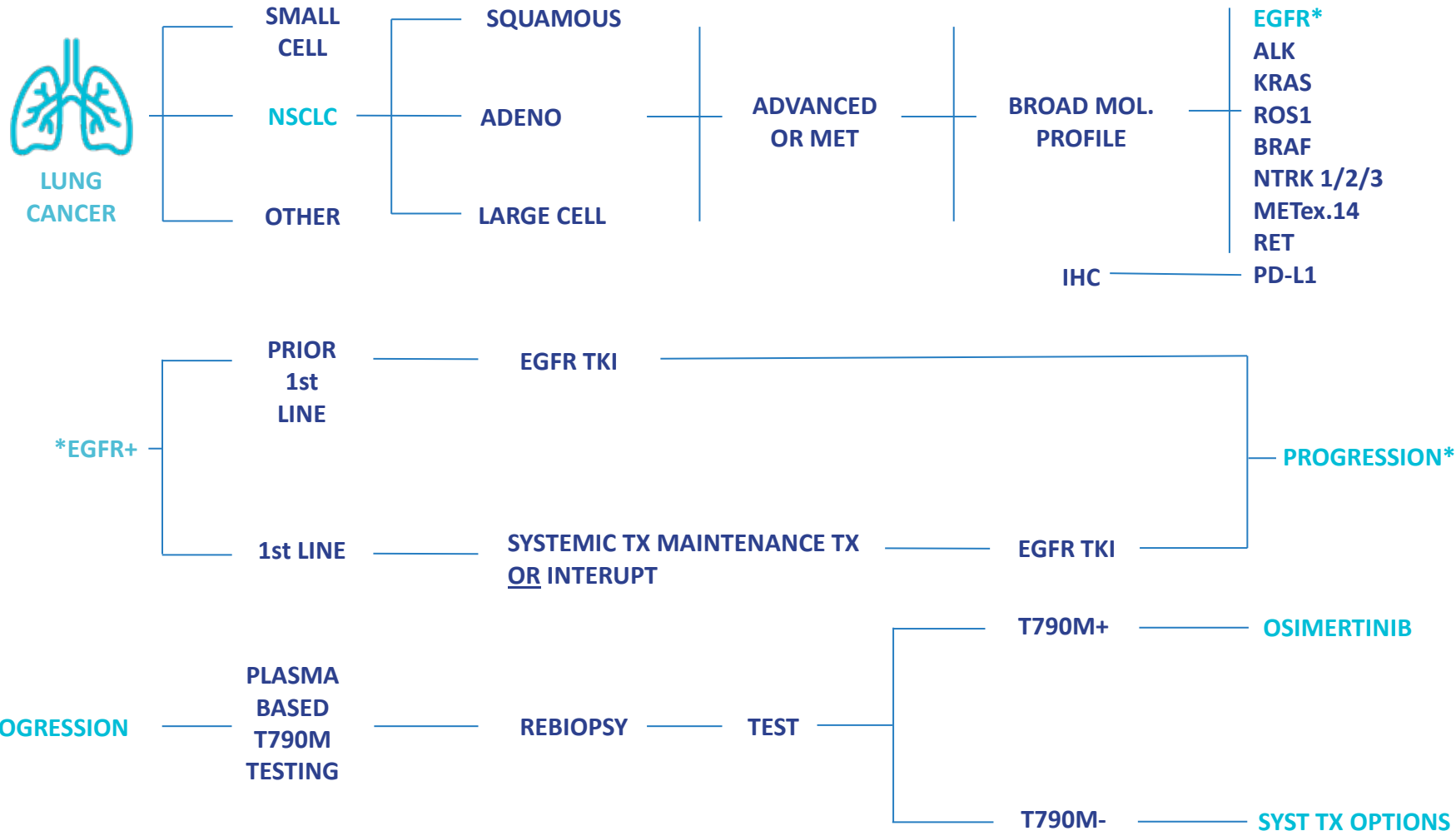Precision Medicine In
Practice For NSCLC

What Is The Future Of NSCLC?

1,200+ NSCLC Related Treatments In The Works

- A pipeline of **1,200+ lung related treatments** in the works.

- There are **2,400+ ongoing clinical trials** globally.

- The next decade will see research partners and the pharmaceutical industry/biotechs face challenges in turning a range of promising scientific ideas into safe, effective medicines to extend the lives of cancer patients.

- **Precision** oncology trials based on cancer **biomarkers** have the potential to improve outcomes by guiding the optimal choice of therapies for patients.

Source Globaldata.com (NSCLC, Phase I-IV, Ongoing Trials, All Sponsor Types)

Where Are Oncology Trials Going?

Precision Medicine, Umbrella Trials, Bucket Trials & Adaptive Design

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LUNG CANCER
- SMALL CELL
- **NSCLC**
  - SQUAMOUS
  - ADENO
  - LARGE CELL
- OTHER

ADVANCED OR MET → BROAD MOL. PROFILE
- **EGFR***
- ALK
- KRAS
- ROS1
- BRAF
- NTRK 1/2/3
- METex.14
- RET

IHC — PD-L1

*EGFR+
- PRIOR 1st LINE — EGFR TKI
- 1st LINE — SYSTEMIC TX MAINTENANCE TX OR INTERUPT — EGFR TKI
→ **PROGRESSION***

*PROGRESSION
- PLASMA BASED T790M TESTING — REBIOPSY — TEST
  - T790M+ — OSIMERTINIB
  - T790M- — SYST TX OPTIONS

NCCN guidelines 2021

02

IHC

IHC Is An Important Screening Tool
From Biopsy To Appropriate Treatment Selection

PD-L1 expression
high

PD-L1 expression
low

Cerba Research Data In-house
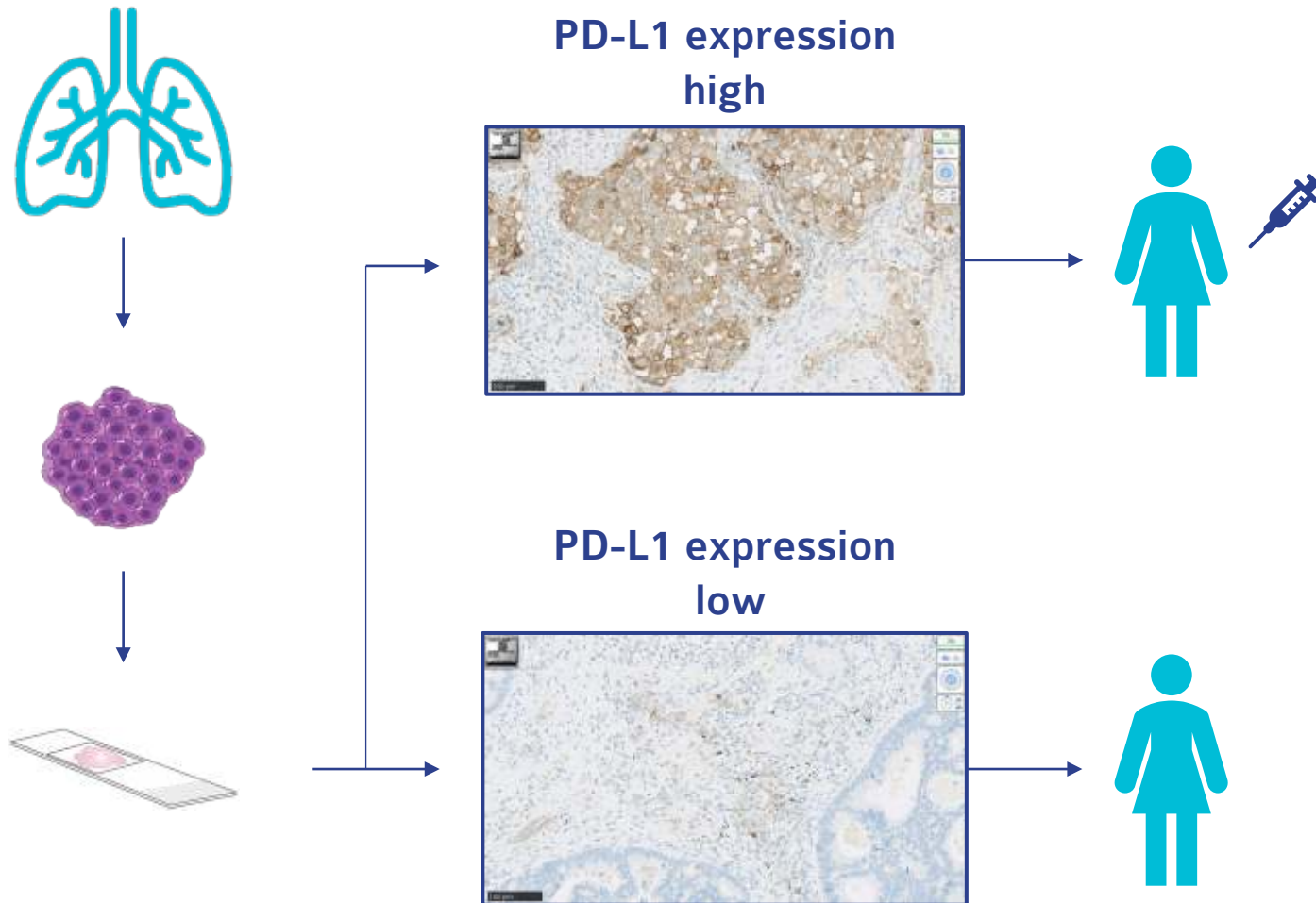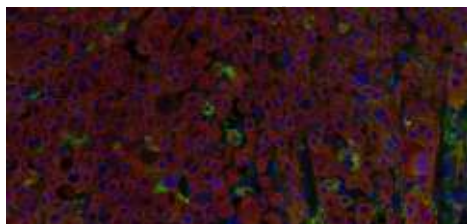
Histopathology
Fully Integrated Process

Design of IHC Protocols
~**200 biomarkers** available* on human tissues
Ability to **customize** projects according to your needs

IHC
Simplex & Multiplex (up to 8 per slide)

panCK (red), PD-L1 (green), CD68

From pre-clinic to clinic
Design & Analytical **Validation**

Central Lab Services

Biobanking
Access to a **wide range** of healthy & pathological tissues
>**3000 blocks** and growing
Tumor microarrays
Storage & distribution of specimens

Pathology
International **network** of board certified pathologists & consultants
1-3 pathologists agreement
Digital pathology

Image Analysis
Transforming visual results into **quantifiable** data

*Cerba Research Data In-house; *Validation level and tissue availability may vary.*

Histology: From Tissue Prep To Analysis

Custom Protocol Development & Validation, Driven By Science Team
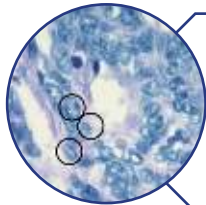

Sample preparation
- Trimming when required
- Tissue processing (dehydration of tissue)
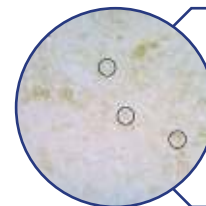- FFPE or fresh frozen embedding
- Sectioning

Staining
- Histology staining (ex. H&E)
- Simplex and multiplex IHC (chromogenic or fluorescence)
- Pre-clinic to clinically validated
- ISH staining

Digitalization
- Digitalization of fluorescent (up to 8 colors) and chromogenic slides
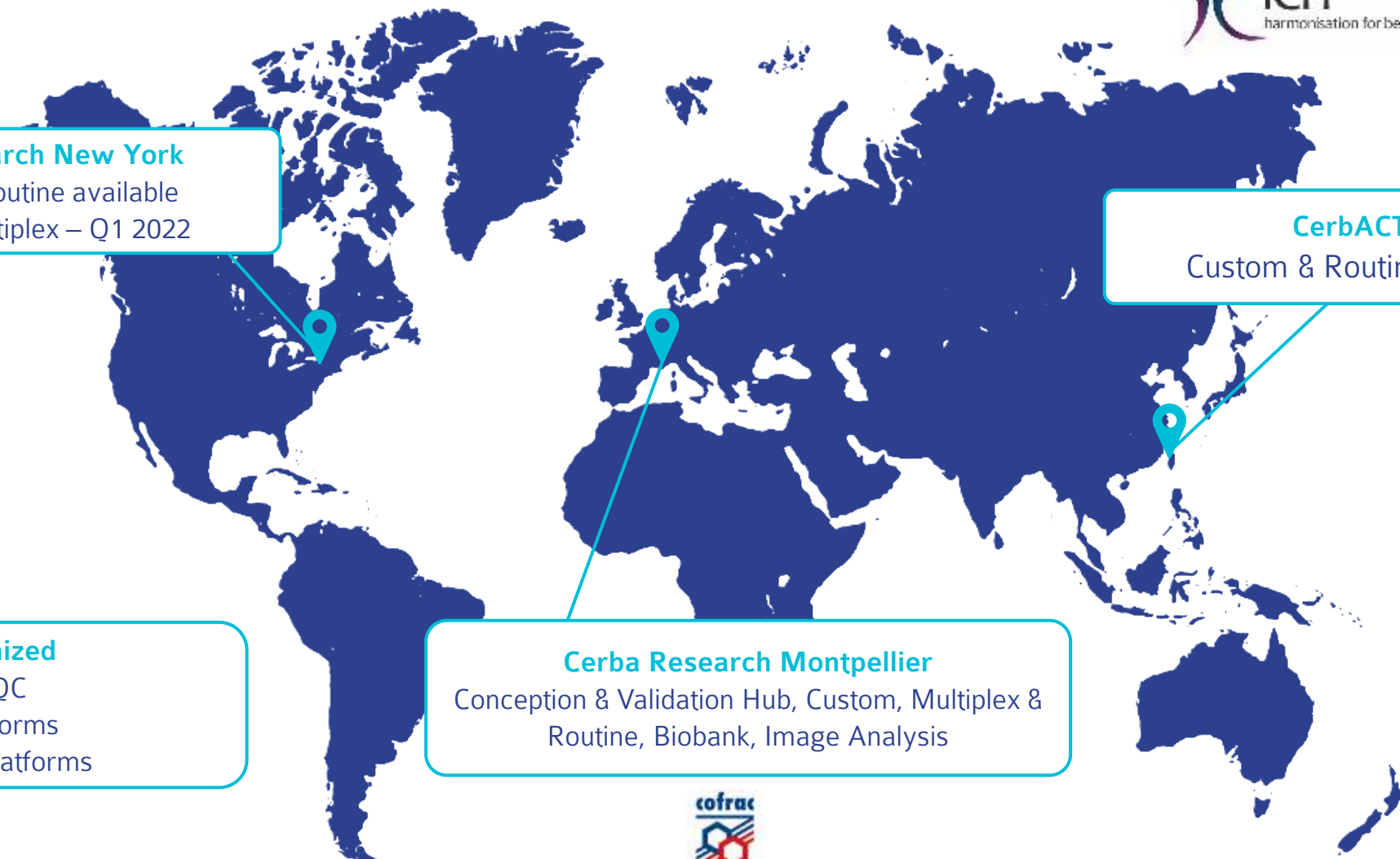- Digital slide sharing (secured)

Scoring, Diagnosis, Analysis
- By pathologists (central reading)
- Image analysis (Halo, Visiopharm)

Harmonized IHC On A Global Scale
Different Sites, Comparable Results

ICH6-GCP quality standards

Cerba Research New York
Diagnostic Routine available
Custom & Multiplex – Q1 2022
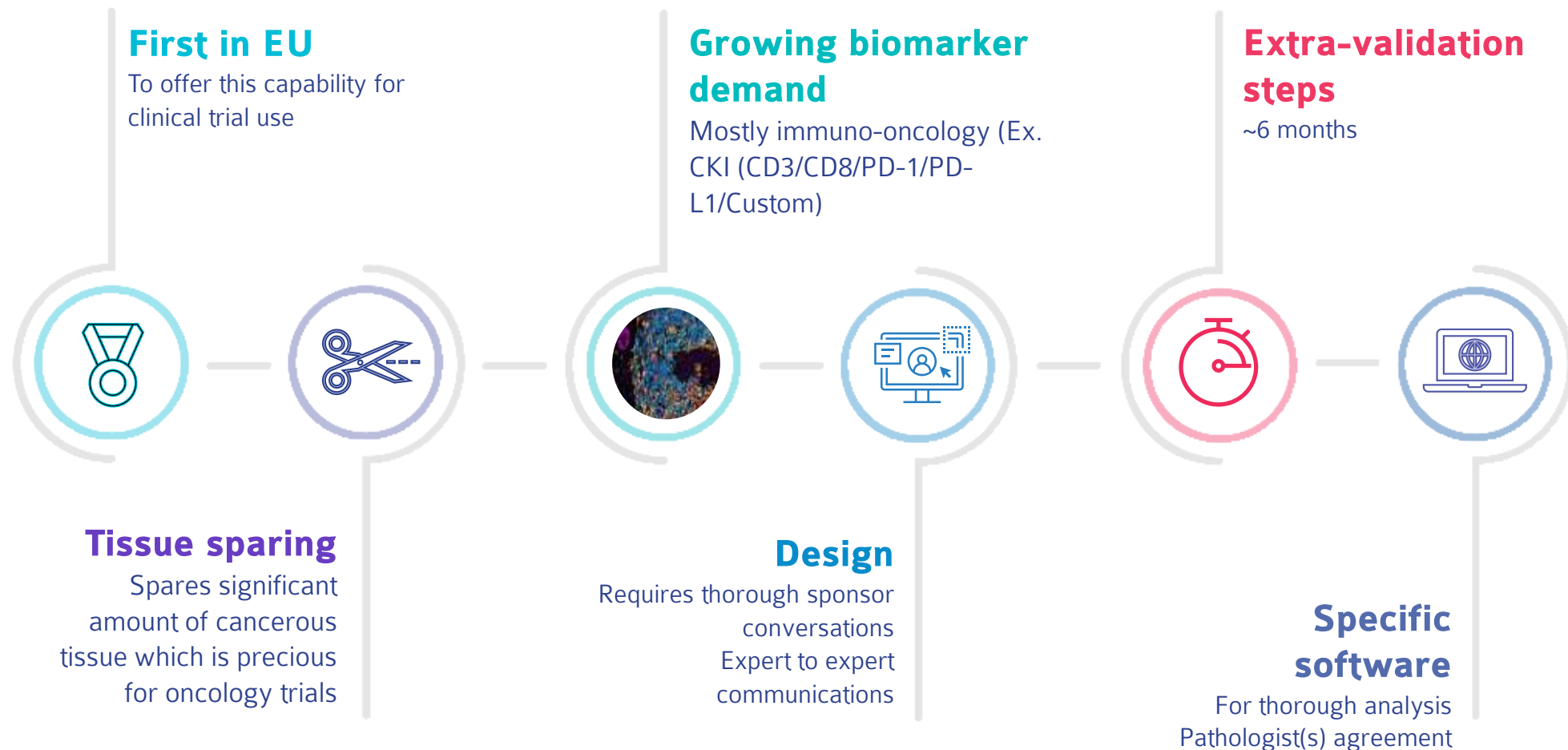
CerbACT Asia
Custom & Routine – Q1 2022

Harmonized
SOP/QC
IHC platforms
Scanning platforms

Cerba Research Montpellier
Conception & Validation Hub, Custom, Multiplex &
Routine, Biobank, Image Analysis

Multiplex IHC
Cerba Research Montpellier

First in EU
To offer this capability for clinical trial use

Growing biomarker demand
Mostly immuno-oncology (Ex. CKI (CD3/CD8/PD-1/PD-L1/Custom)

Extra-validation steps
~6 months

Tissue sparing
Spares significant amount of cancerous tissue which is precious for oncology trials

Design
Requires thorough sponsor conversations
Expert to expert communications

Specific software
For thorough analysis
Pathologist(s) agreement

Cerba Research Data In-house. Validation level and tissue availability may vary.

Examples Of Cerba Research IHC Available Targets
To Name A Few & With Many Actionable Targets

CKI/immuno-oncology
PD-1, PD-L1, Treg*, Treg light*, **CKI*, PD-L1 panel*,** Neutrophil Elastase

Liquid tumors
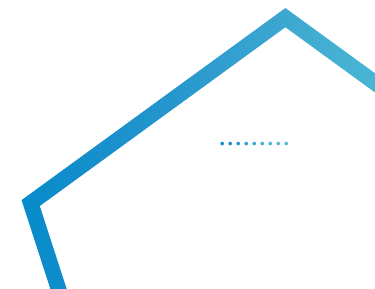Lambda, Kappa, CD3,4,8,11b,30,45,47,56,68,123,137,138,226, TCF4*, Treg*, NK cells*

Lung
PD-1, PD-L1, EGFR, ALK, cMet, IL-1$^{\alpha}$, Nkp46, FoxP3, SIRPa, Treg*, MDSC*, NK cells*

Breast
ER, PR, HER2, PD-L1, PD-1, CK7, Cytokeratin19, P-AKT, Treg*, NKp46

Colorectal
PD-1, PD-L1, CEA, NKp46, Treg*, VEGFR/CEA*, p53, **PD-L1**/CD68*, **PD-1**/CD3*

*Cerba Research Data In-house. Validation level and tissue availability may vary. **Bold**=targetable.*Multiplex panel*

Examples Of Cerba Research IHC Available Targets
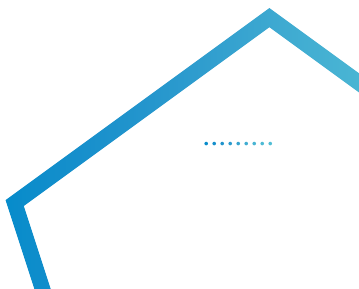## To Name A Few & with Many Actionable Targets

Liver – HCC
PD-1, adipophilin, cleaved caspase 3, CD11b,31,56,68,163, NKp46, Treg*

Pancreatic Cancer
PD-L1, PD-1, CD8,25,56,68,163, IL-1$^\alpha$, NKp46, NK cells*

GyneOnc
PD-L1, PD-1, NKp46, CD11b,47, Treg*

Tumor Markers
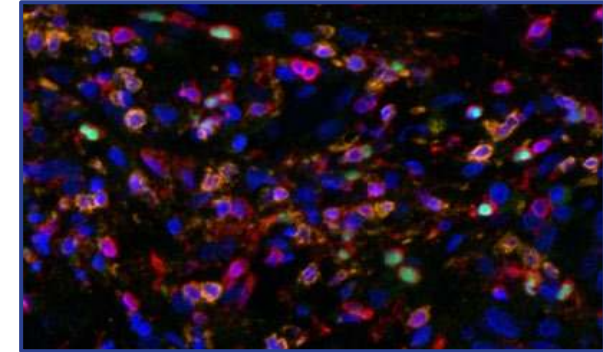p53, p63, p21, Ki-67, Cytokeratin
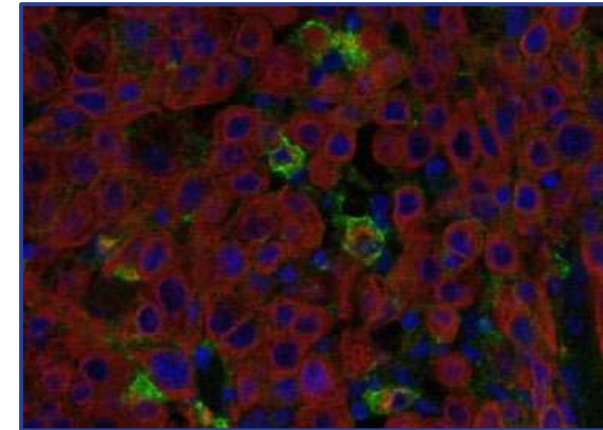
And more...
According to your needs

A Rich Immuno-oncology Multiplex Panel
Histoprofile®

- T reg (CD3/CD4/CD8/CD25/FoxP3)
- T reg light (CD3/CD8/FoxP3)
- M1/M2 (CD68/CD163/c-maf/pSTAT1)
- CKI (CD3/CD8/PD-1/PD-L1/Custom)
- PD-L1 panel (CD68/panCK/PD-L1)
- Tumor temp (CD3/CD8/Tumor mask) – Chromogenic or Fluorescent
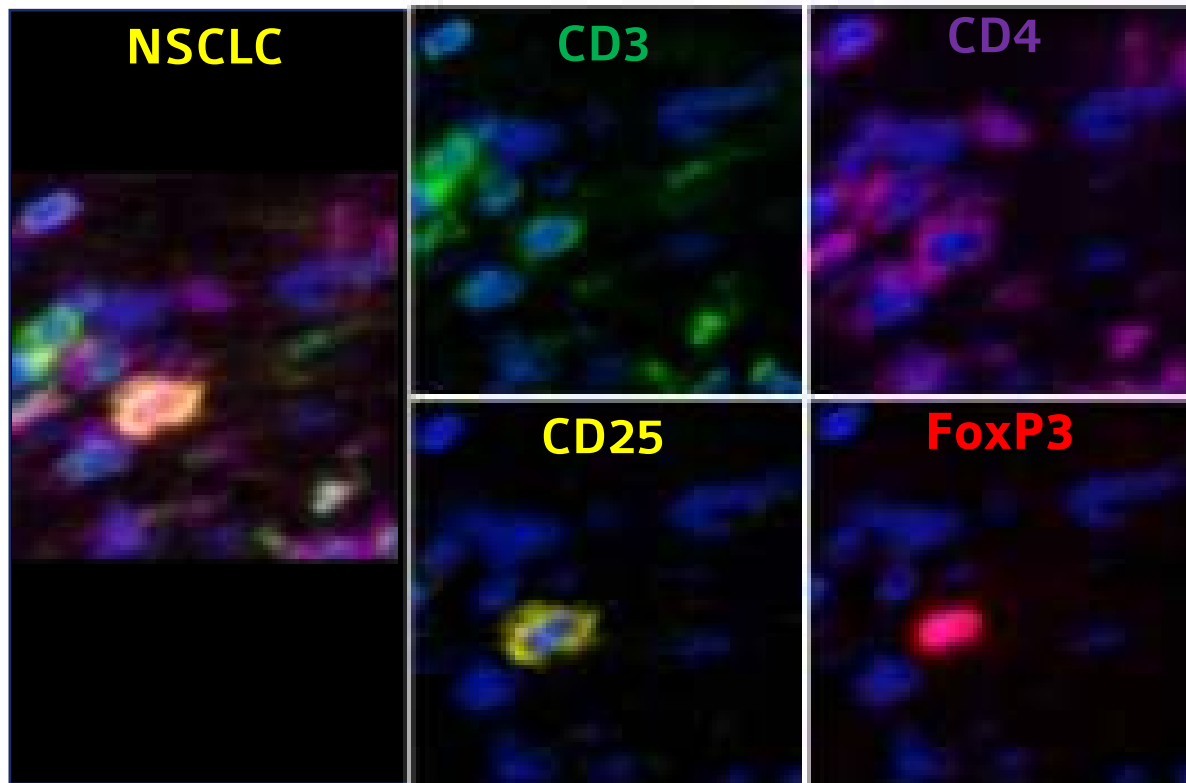- TRM (CD3/CD8/CD103/CD69/CD49a)

T reg light, HNSCC (larynx)

PD-L1 panel, NSCLC

Cerba Research Data In-house. Validation level and tissue availability may vary.

A NSCLC Multiplex Panel Example

Histoprofile®–Treg

CD3/CD8/CD4/CD25/FoxP3 expression

Specimen NSCLC FFPE

Platform Leica Bond Rx

Pre-validated Lung
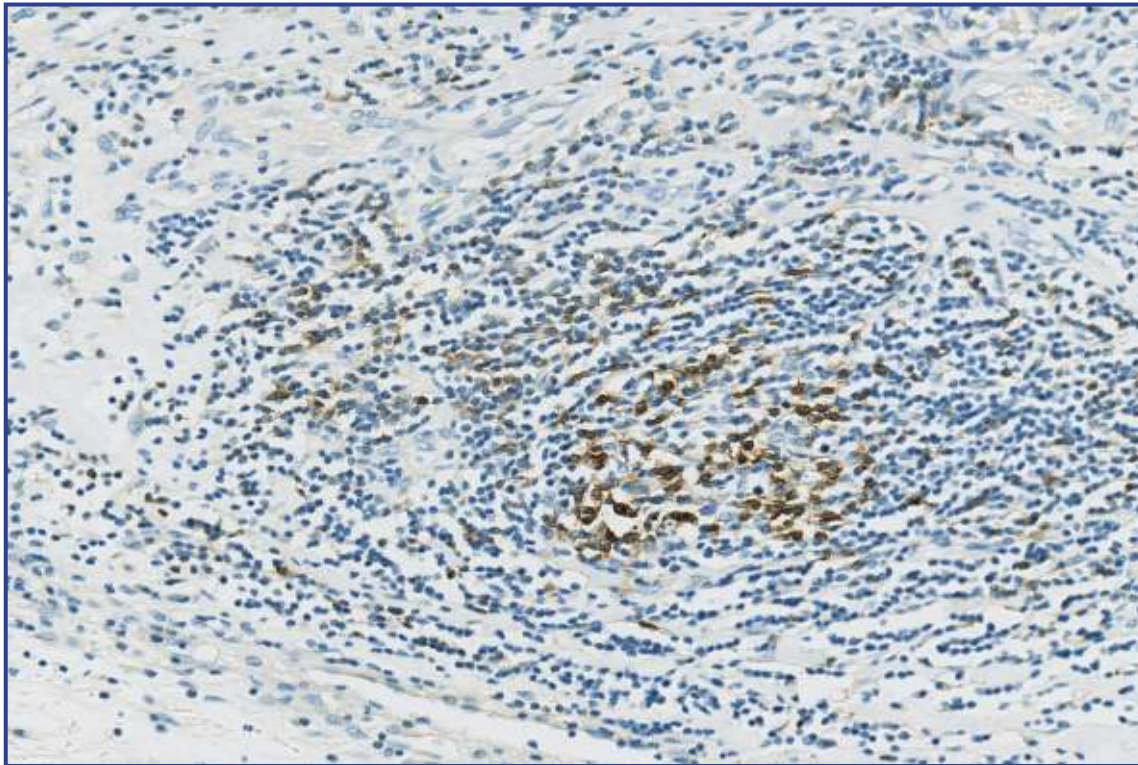**tissues** Various solid tumors

Ab CD3 (2GV6, Roche)
CD8 (4B11, Thermo Fisher)
CD4 (EPR6855, abcam)
CD25 (4C9, Leica)
FoxP3 (236A/E7, abcam)

Cerba Research Data In-house. Validation level and tissue availability may vary. Courtesy of Elena Baranova, PhD

Cerba Research

Strong Immuno-oncology IHC Results
We Deliver Reliable, Reproducible Results

Cerba Research

PD-1 expression present

Specimen	Lung FFPE
Platform	Benchmark Ultra
Validated tissues	Lung
	Breast
	Ovary
	Pancreas
	Gastric
Ab	PD-1 (NAT105, Roche)

Next Generation IHC/ISH Multiplexing
Maximize Your Clinical Trial Success

Cerba Research

Maximum data per tissue
Tissue sparing

Co-expression & spatial organization
Multiple targets within preserved tissue architecture

From pre-clinical to clinical
Capacity to offer relevant markers for your trial strategy

Immune Profiling
Characterization of the tumor
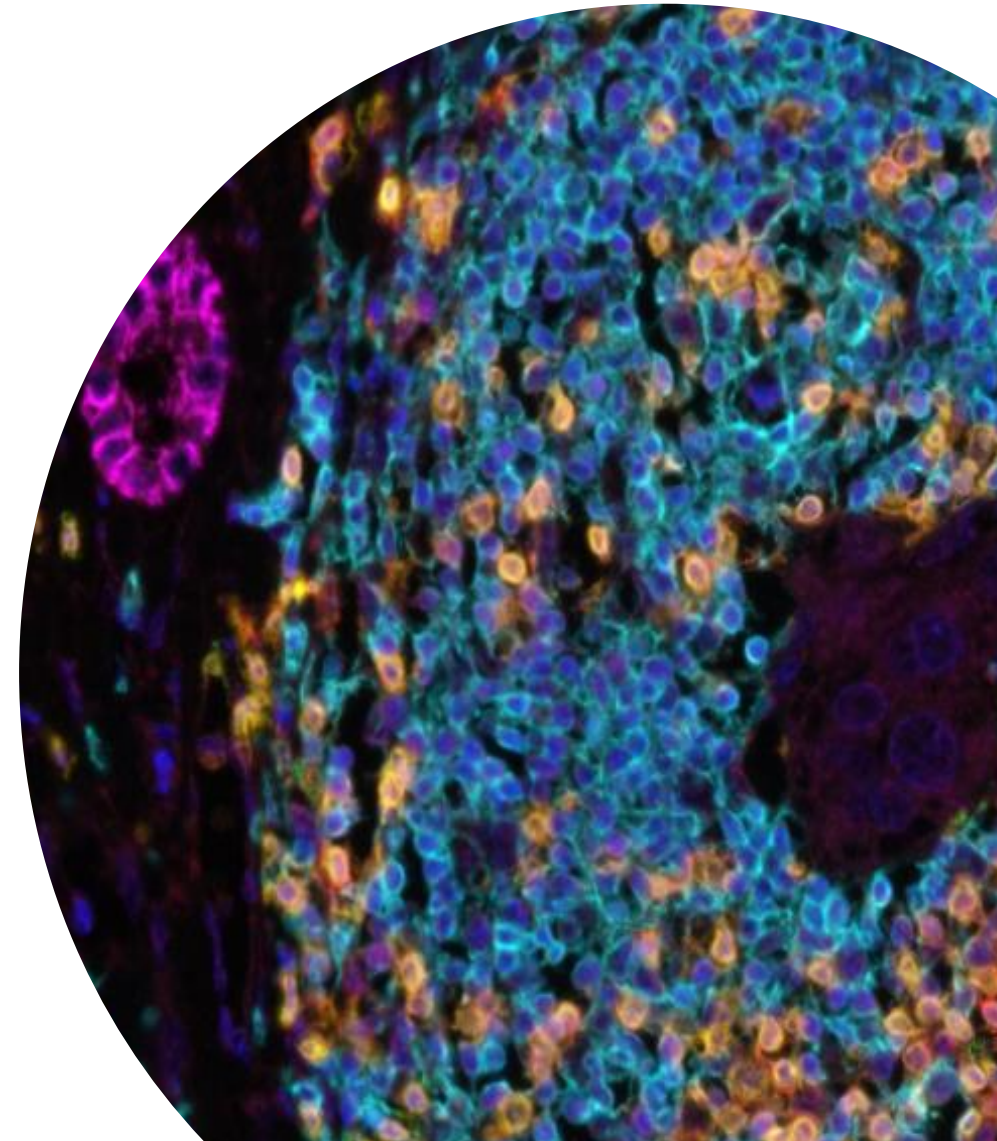
03

NGS

From Sample Collection To Select Treatment

What is NGS?

NGS Broad panel assay (e.g.oncopanel)

Identification of gene defect(s) DNA/RNA → ALK+ →

ALK inhibitor
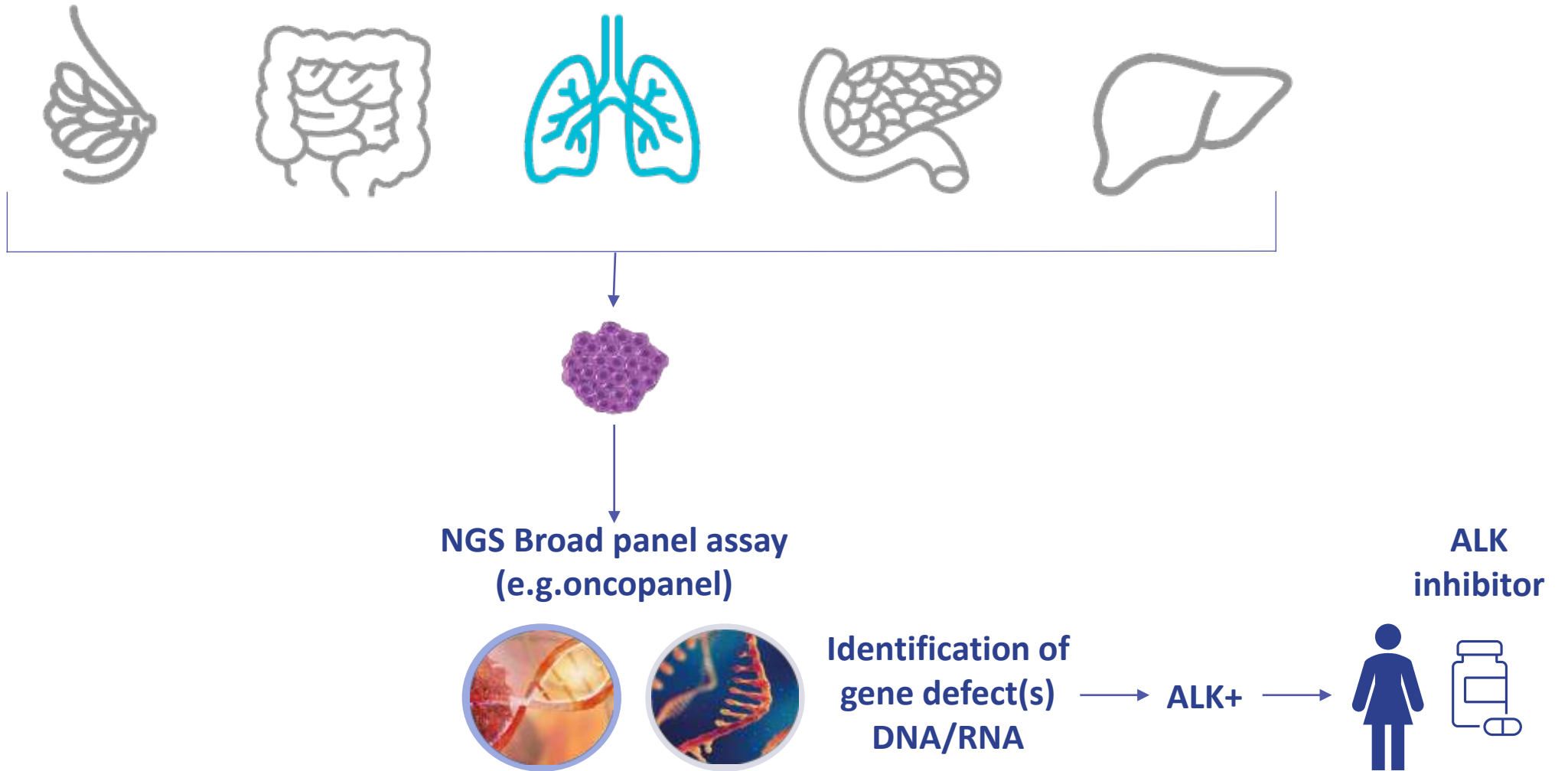
What Are Guidelines Proposing For NGS?
NSCLC

Biomarker	Preferred Assay	Additional Assays
EGFR	NGS	RT-PCR, Sanger sequencing
ALK	NGS, IHC	FISH
ROS1	NGS, IHC	FISH
BRAF	NGS	RT-PCR, Sanger sequencing
KRAS	Not specified	
MET	NGS	
RET	NGS	FISH, RT-PCR
NTRK1/2/3	NGS, IHC	FISH, PCR
EGFR T790M	Not specified	
PD-L1	IHC	

NGS with a broad panel (e.g. oncopanels)

Most commonly used testing method in clinical practice

NCCN guidelines 2021; Bebb et al. Curr Oncol 2021

Our NGS Workflow
From Sample Collection To Reporting
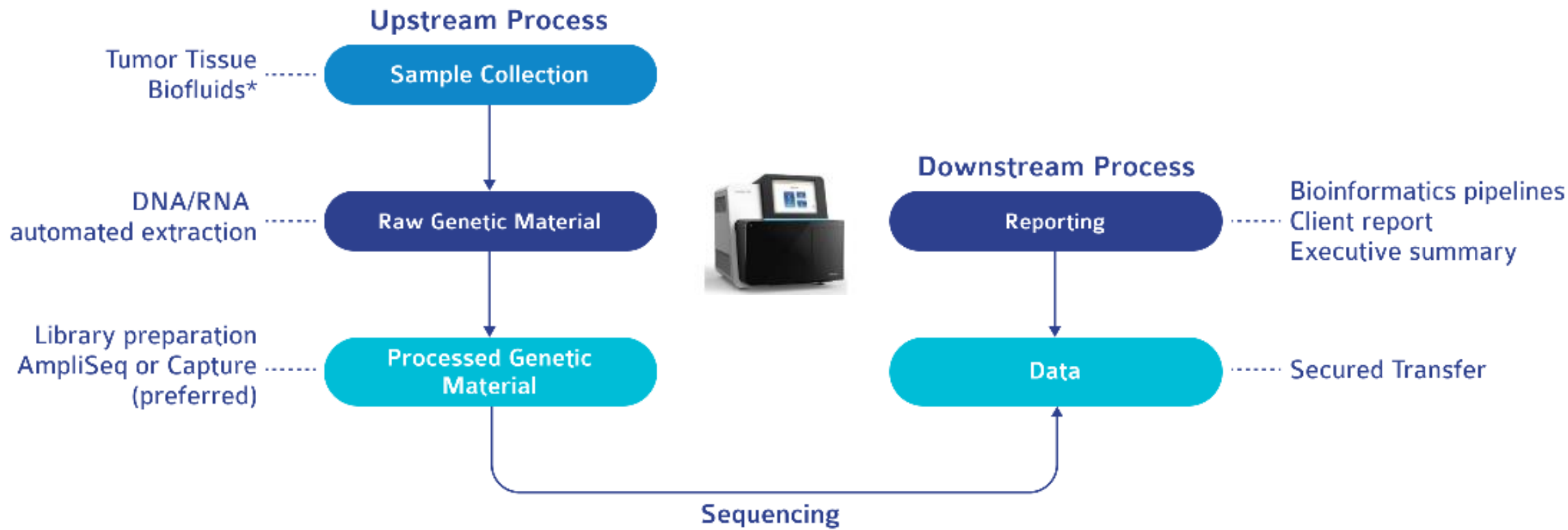
Cerba Research Data In-house: *can be FFPE, fresh frozen, cell-free DNA, ctDNA

NGS Capabilities On A Global Scale
Different Sites, Comparable Offerings

Cerba Research

Tawain Laboratory
Ion Torrent & Illumina
Custom panels, Oncopanels

US Laboratory
Illumina Platform
Custom panels, Oncopanels

Cerba Paris
Illumina Platform
Custom panels, Oncopanels

Belgium Laboratory
Illumina Platform
NGS RNAseq, Oncopanels (under dev)

Cerba Research Data In-house; whole genome/whole exome/RT-PCR/qPCR also available if needed
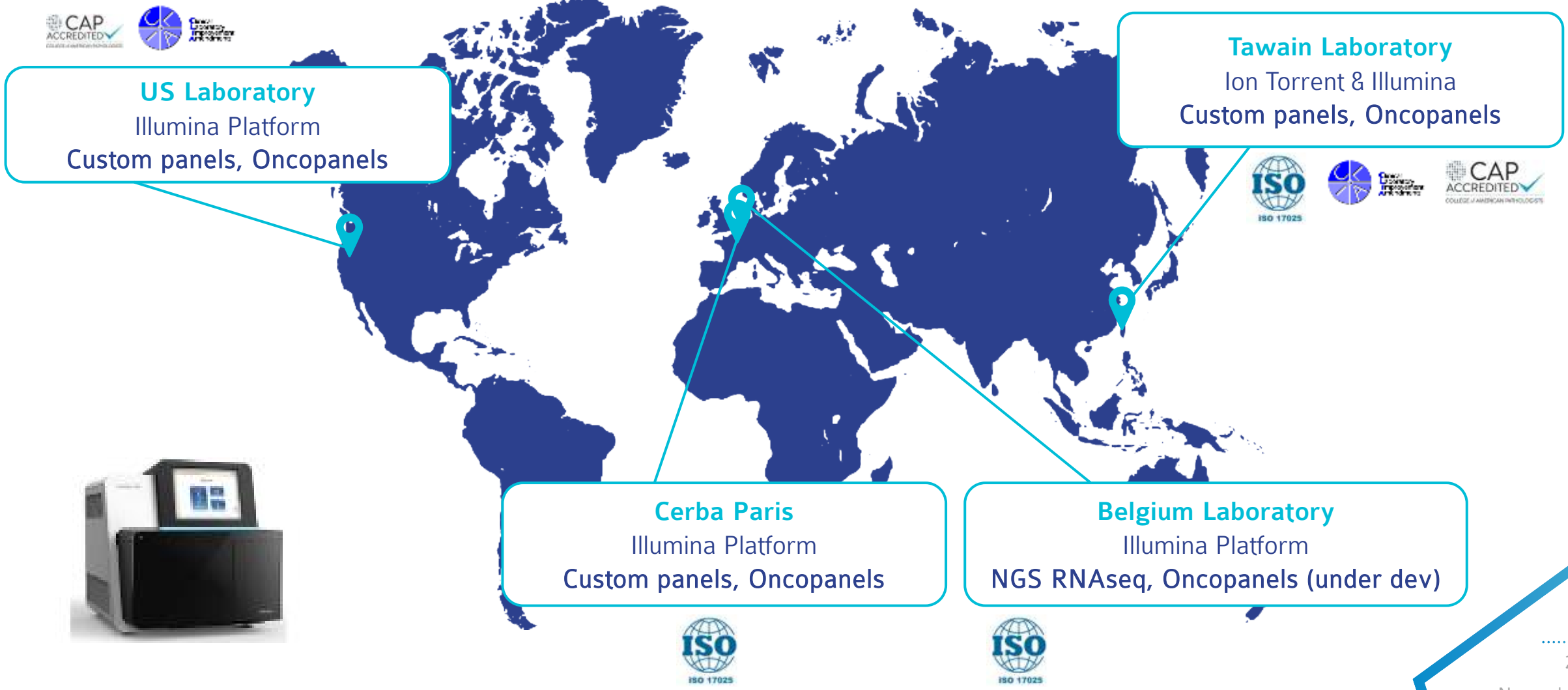
Our Typical Turnaround Time For Existing Oncopanels
Customize A Panel According To Your Trial Needs
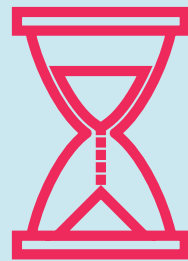
Turnaround Time

2-3 weeks*

Customizable

Add additional cancer genes or create a panel

*Cerba Research Data In-house; *from receipt of approved samples to result*

Comprehensive Oncopanels Available For Analysis
Cerba Paris

Cerba Research

	Genes	Tumor Type	Instrument	TAT*	Bone marrow	Peripheral blood	FFPE
✓ EGFR, KRAS, BRAF, HER2 & PIK3CA	5	Solid tumors	NextSeq	15			x
✓ KRAS & NRAS	2	Solid tumors	NextSeq	15			x
✓ EGFR, KRAS & BRAF	3	Solid tumors	NextSeq	15			x

*Cerba Research Data In-house; *(days) from receipt of approved samples to result*

Comprehensive Oncopanels Available For Analysis
Cerba Paris

	Genes	Tumor Type	Instrument	TAT*	Bone marrow	Peripheral blood	FFPE
✓ BRAF & NRAS	2	Solid tumors	Next Seq	15			x
✓ BRAF, KRAS & NRAS	3	Solid tumors	Next Seq	15			x
✓ BRAF, NRAS & KIT	3	Solid tumors	NextSeq	15			x
✓ EGFR & KRAS	2	Solid tumors	NextSeq	15		x (EGFR)	x

*Cerba Research Data In-house; *from receipt of approved samples to result*

Comprehensive Oncopanels Available For Analysis

Cerba Paris

	Genes	Cancer Type	Instrument	TAT*	Bone marrow	Peripheral blood	FFPE
Routine panel (under dev)**	37 DNA 17 RNA	Pan-cancer	NextSeq	NA			x
TruSight Oncology 500-like (under dev)**	523 DNA 55 RNA	Pan-cancer	NextSeq	NA			x

*Cerba Research Data In-house; *(days) from receipt of approved samples to result; **DNA=37 genes (SNVs, Indels, CNVs)+microsatellites & RNA= 17 gene fusions; ***DNA=523 genes (SNVs, Indels, CNVs)+microsatellites+tumor mutational burden & RNA=55 gene fusion*

Comprehensive Oncopanels Available For Analysis

Tawain Laboratory

Cerba Research

|	Genes	Cancer Type	Instrument	TAT*	Bone marrow	Peripheral blood	FFPE
ACTOnco®+ (DNA-based) ✓	440	Solid tumors (important hallmarks of cancer)	Ion Torrent	10			x
ACTDrug® (DNA-based) ✓	40	Solid tumors (screening of actionable genes)	Ion Torrent	10			x
ACTFusion™ (RNA-based) ✓	31	Solid tumors (actionable fusion genes)	Ion Torrent	10			x
ACTHRD™ (DNA-based) ✓	24	Solid tumors (gene alterations to evaluate PARP inh)	NextSeq 550	10			x

*Cerba Research Data In-house; *(days) from receipt of approved samples to result*

Comprehensive Oncopanels Available For Analysis
Belgium Laboratory

Cerba Research

	Genes	Tumor Type	Instrument	TAT*	Bone marrow	Peripheral blood	FFPE
TruSight Oncology 500 (DNA/RNA) (under dev)	523	Solid tumors	NextSeq	NA			x
TruSight Oncology 500 High throughput (DNA/RNA) (under dev)	523	Sample batching (16-192) pan-cancers	NovaSeq	NA			x

*Cerba Research Data In-house; *(days) from receipt of approved samples to result*
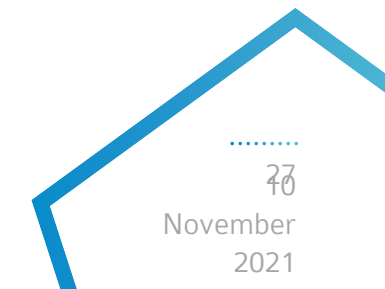
Create Your Project With Customizable Panels In Mind
Plan Your Project With Our Bioinformaticians and Scientists

Knowledgeable
NGS-based genetic testing
Solid & liquid tumors

Agile
According to your trial
needs

Customizable
Add new genes or create a
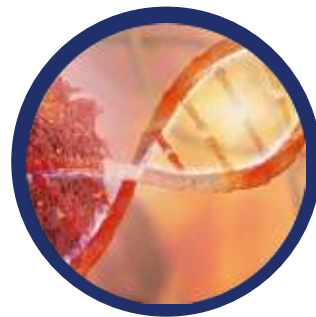new panel

Turnaround time
Fast and efficient
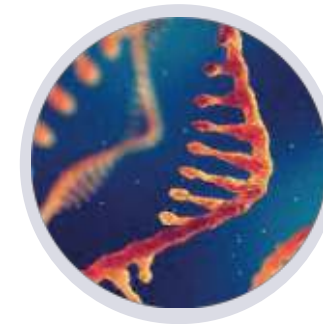
What Is ctDNA?
Liquid Biopsy

ctDNA (also interchangeable with "circulating cell-free tumor DNA") are fragments of DNA found in the bloodstream.

Candidate nucleic acid biomarkers in plasma
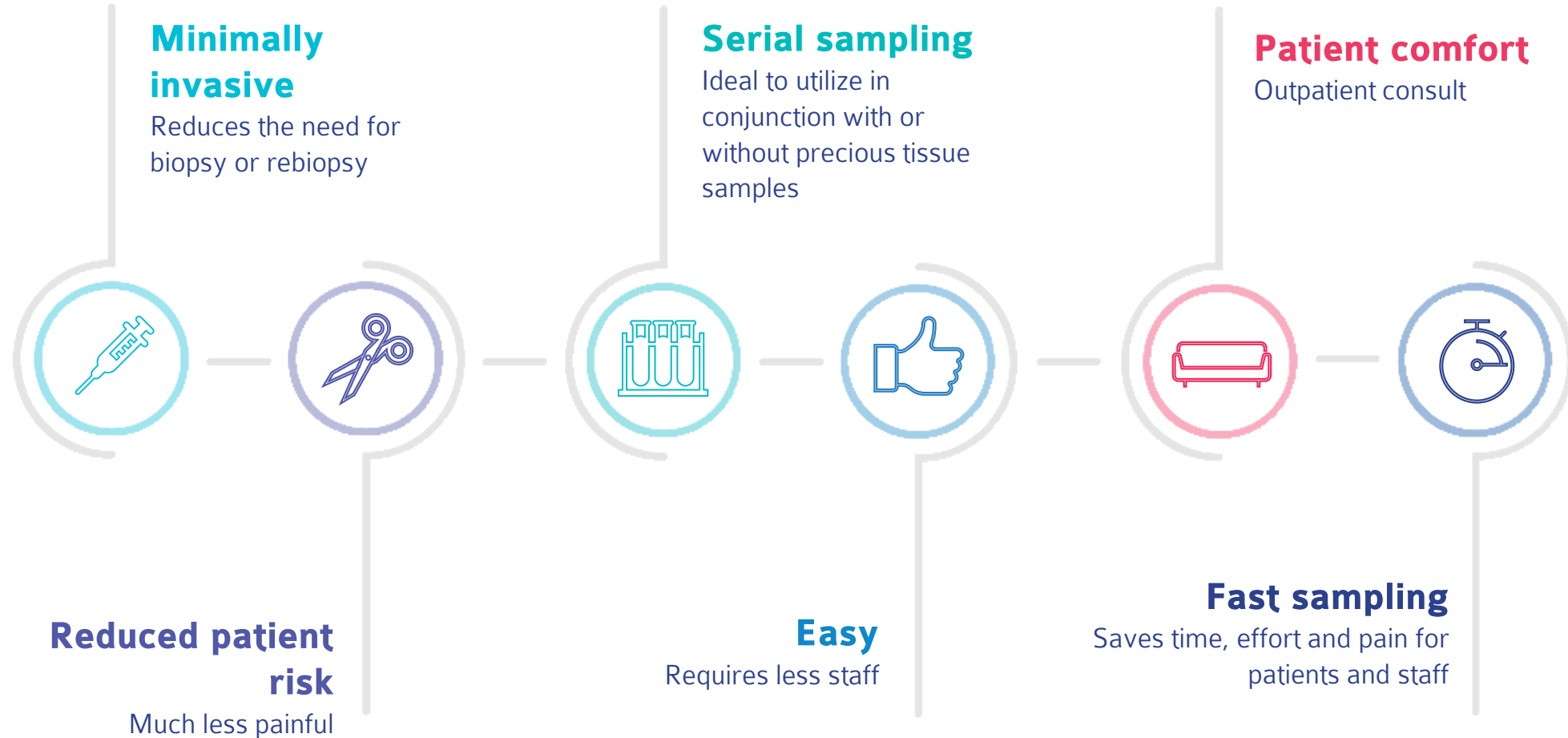
DNA

Extracellular cell-free circulating DNA

RNA

mRNA
Micro-RNA
Long non-coding RNA

Advantages Of Liquid Biopsies

An Alternative To Tissue Biopsy

Cerba Research

Minimally invasive
Reduces the need for biopsy or rebiopsy

Serial sampling
Ideal to utilize in conjunction with or without precious tissue samples

Patient comfort
Outpatient consult

Reduced patient risk
Much less painful

Easy
Requires less staff

Fast sampling
Saves time, effort and pain for patients and staff

Cerba Research Data In-house

ctDNA Capabilities On A Global Scale
Different Sites, Comparable Offerings

US Laboratory
ctDNA

Tawain Laboratory
ACTMonitor®

Cerba Paris
ctDNA (T790M)

Belgium Laboratory
Under development

Cerba Research Data In-house; whole genome/whole exome/RT-PCR/qPCR also available if needed

What Is Needed For The Collection Of ctDNA?

Direct-draw Venous Whole Blood Collection Devices

- ctDNA is isolated from plasma derived from anti-coagulated peripheral whole blood of cancer patients.

- There exists several direct draw whole blood collection tubes intended for collection, transport and storage of blood samples.

- Usually contains the anticoagulant K_2EDTA and a cell preservative in a liquid medium.

- We are using **Streck tubes** dedicated to the preservation of cell-free DNA.

- We are also using **PAXgene® blood RNA tubes** which are intended for immediate stabilization of intracellular RNA.

Our Capabilities For NGS ctDNA
Cerba Paris & Belgium Laboratory

	Genes	Tumor Type	Instrument	Lab	TAT*	Liquid biopsy
✓ **EGRF T790M**	1	Lung cancer	Roche Cobas	Cerba Paris	15	x
TruSight Oncology 500 ctDNA (ctDNA-based) (under dev)	523	Pan-cancers	NovaSeq	Belgium	TBD	x

Cerba Research Data In-house

Comprehensive Oncopanels Available For Analysis
Tawain Laboratory

Cerba Research

	Genes	Tumor Type	Instrument	TAT*	Liquid biopsy
✓ **ACTMonitor®** **(ctDNA—based)** ✓	50	Solid tumors (uses ctDNA to provide an early detection of cancer recurrence & drug resistance)	Ion Torrent	10	x
ACTMonitor® Lung **(ctDNA—based)**	11	Lung (monitors lung cancer recurrence & drug resistance)	Ion Torrent	10	x

*Cerba Research Data In-house; *(days) from receipt of approved samples to result*

In Conclusion

Our Precision Medicine Involvement In NSCLC And Beyond

Cerba Research

DNA
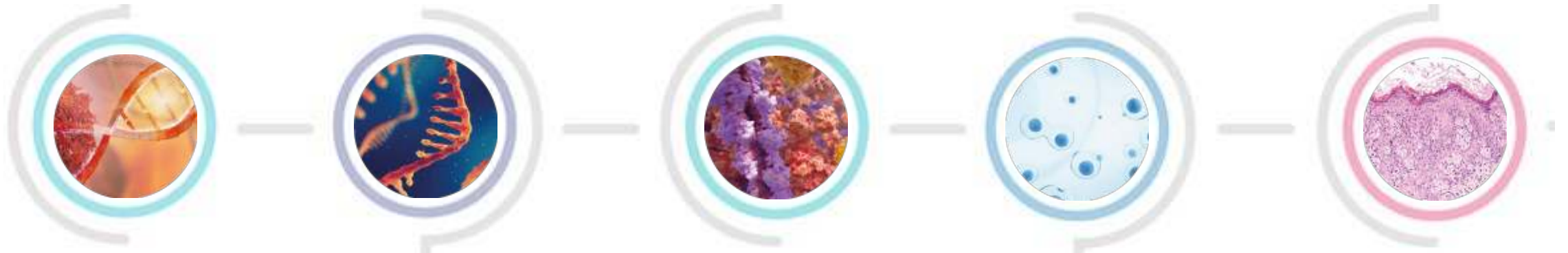
NGS
Oncopanels
Custom panels
ctDNA

PCR-ddPCR,
qPCR
Whole exome
Whole genome

RNA

RNAseq
rtPCR

Protein

Multiplex cytokine
profiling
Custom ligand
binding assays-ELISA,
etc.

Cell

FCM
NGF under dev (up to 40
colors)
Immunophenotyping
Receptor occupancy
MRD Quantification
Marker analysis (cell
surface/cytoplasmic)
CAR T cell detection &
enumeration

Tissue

Multiplex/Simplex IHC
200+ biomarkers/protocols
Centralized pathology
reading
FISH, ISH protocols
Strong immuno-onc
simplex & multiplex panels
Spatial analysis in the
tumor microenvironment

Cerba Research Data In-house

Thank you!

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