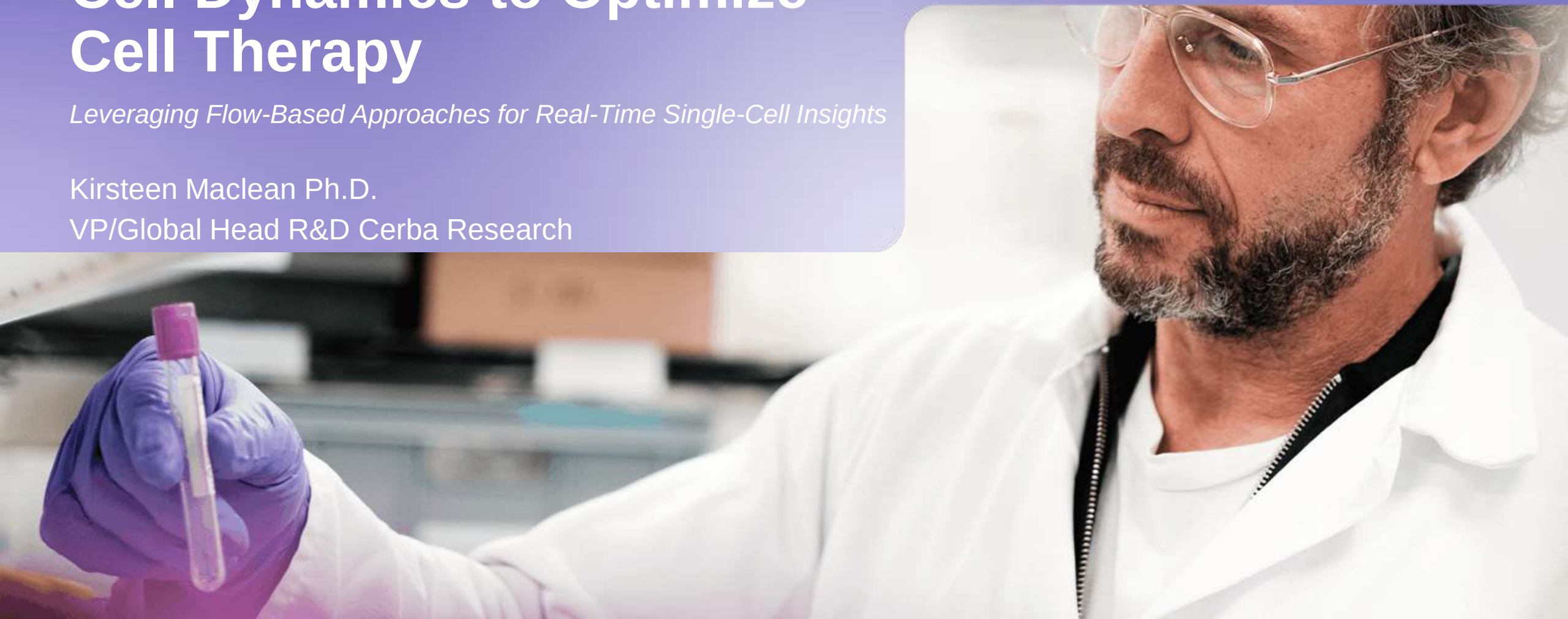
Presentation Deck

Cerba Research

Mapping Killer and Bystander Cell Dynamics to Optimize Cell Therapy

Leveraging Flow-Based Approaches for Real-Time Single-Cell Insights

Kirsteen Maclean Ph.D.
VP/Global Head R&D Cerba Research



The opportunity: Redefining modern medicine

Cerba Research

Cell therapy, often described as a **"living drug,"** is advancing rapidly across a wide range of disease areas. However, its inherent biological complexity creates analytical, manufacturing, and regulatory challenges that differ significantly from those associated with traditional small-molecule and biologic therapeutics.



Oncology



Rare diseases



Hematology



Regenerative medicine

Testing Challenges

Short Shelf-Life: Autologous cell therapies must be tested and infused quickly before the cells expire.

Complex Potency Assays: MoA is often complex.

Sample Volume: Limits the number of tests you can run.

Product Variability: Changes from patient to patient, making standard baseline testing difficult.

Monitoring Challenges

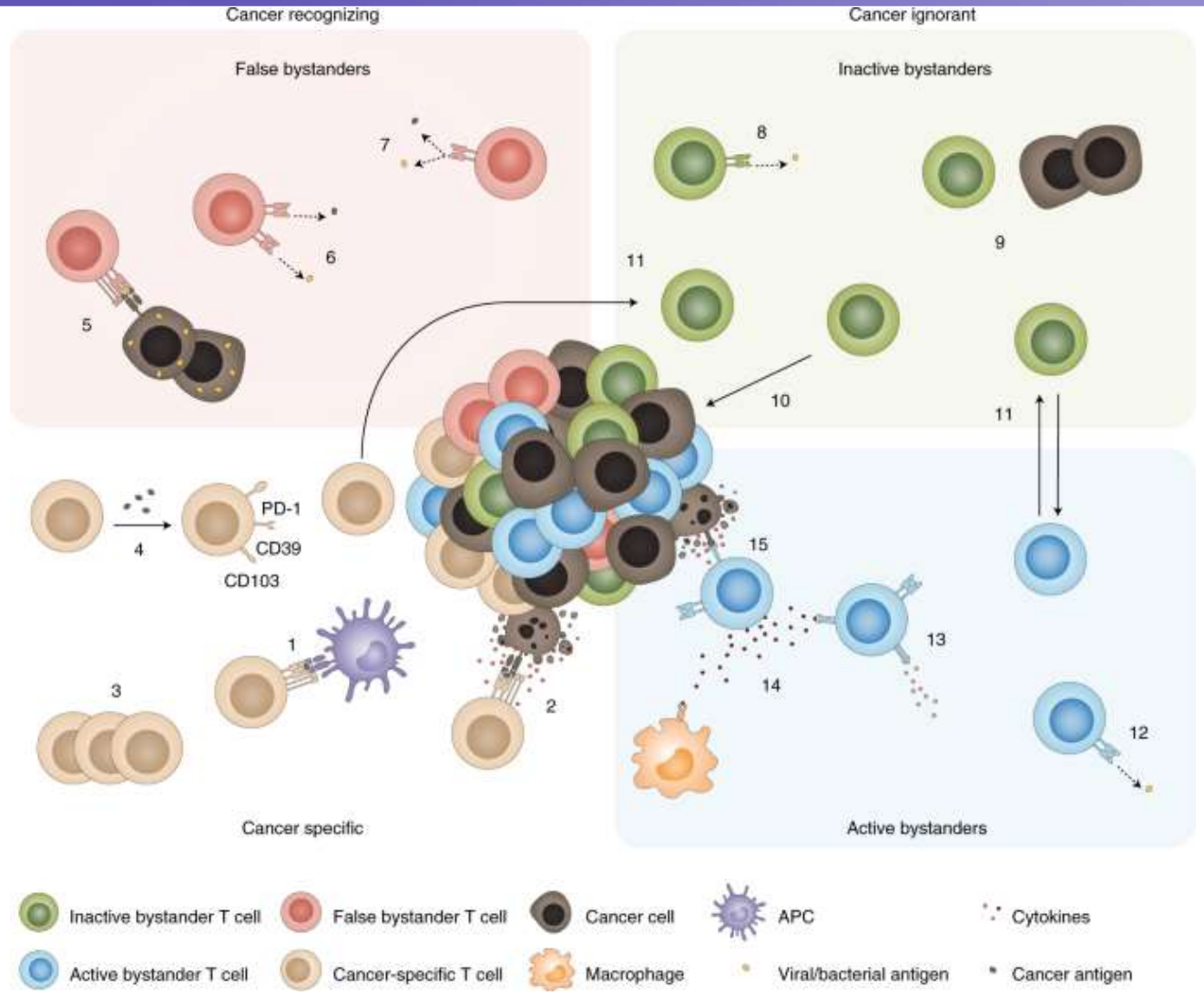
Long-Term Follow-Up: Regulatory require patient tracking for years to check for late side effects or vector persistence.

Immune Reactions: Detecting unexpected immune responses or toxicity,

Vector Shedding: Monitoring viral vector shedding in bodily fluids requires specialized assays to ensure safety for the environment

Mapping CAR T cell dynamics to support the next-generation cell therapy design

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- Mapping killer and bystander cell dynamics allows researchers to improve cell therapy by harnessing un-targeted neighboring cells to clear tumors that evade direct detection
- **Killer Cells**: Cytotoxic T cells or natural killer cells seek out and destroy cells with specific target antigens
- **Bystander Cells**: Neighboring non-targeted cells, such as endogenous CD8+ T cells or macrophages, can be recruited to help attack the tumor

Why Cerba Research: End-to-end Laboratory Solutions

Scientific expertise, agility and scale for optimized solutions



Specialty Laboratory Services

Biomarker Services

- "Off- the-Shelf" panels
- Custom assay development
- Immunoassays
- **Flow Cytometry**
- Molecular testing
- Next Generation Sequencing
- DNA/RNA Extraction and qPCR
- Histopathology
- Cytogenetics
- BSL3 laboratory network

Bioanalytical Services

- Pre-clinical (GLP & non-GLP)
- Clinical (Primary, Secondary & Exploratory endpoints)
- Vaccines, Biologics and Biosimilars
- Full PK & Immunogenicity programs



Central Laboratory Services

- Safety and routine testing
- Global network capabilities
- PBMC Processing

Logistic Solutions for Kit & Sample Management

Standard and Premium Services for complex trials

High quality data harmonized across laboratories - Valid laboratory licenses and accreditations

- Cerba Research operates in Europe through several legal entities that qualify as Health Institutions under IVDR,
- Within these entities, LDTs are designed, manufactured, and used in compliance with the conditions set forth under Article 5(5), including their use under appropriate quality and governance frameworks, in accordance with applicable national requirements.

CGT Highlights Across Therapy Areas

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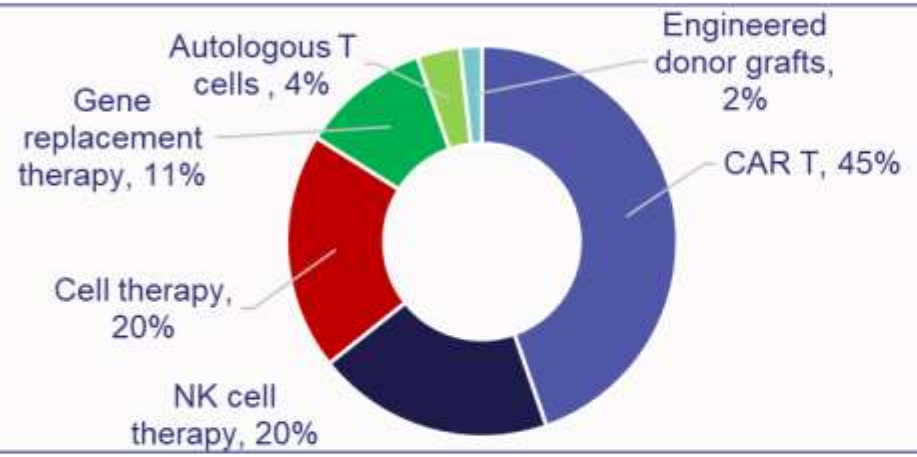
~60
CGT trials since 2018

85%+
Trials include specialty testing

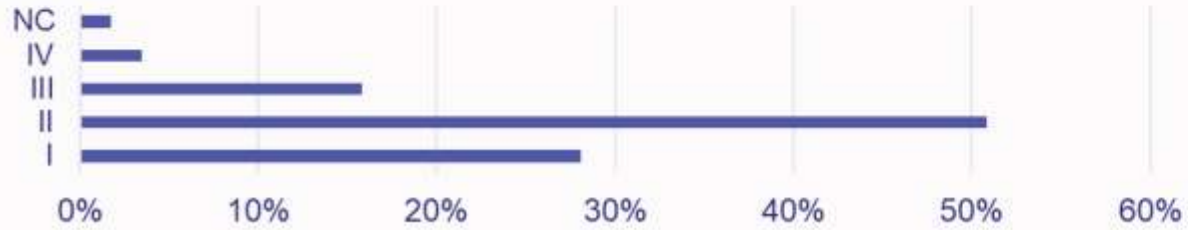
45%
CAR T Driven

~60%
In hematological malignancies

Asset Class



Clinical Trial Phases Overview



Market Authorization / Expansion

7
Market authorizations / expansions

3
CAR T

Approved Indications

- Multiple myeloma (MM)
- Diffuse large B cell lymphoma (DLBCL)
- Epidermolysis bullosa
- Spinal muscular atrophy (SMA)

Cerba Research Data In-house (updated 20Jan2026, excluding Rotterdam & BARC SA); CGT=cell & gene therapy; NK=natural killer; CAR T= chimeric antigen receptor T cell therapy

Approved Cell & Gene Therapies

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Trade name	Active ingredient	Genetic modification method	Vector type	EMA authorized indication / EMA authorization type	FDA authorized indication/ FDA authorization type
Strimvelis®	Ex vivo gene modified cells	Gene addition	Retroviral	Severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)/ conditional approval	No FDA approved indication
Kymriah®	Tisagenlecleucel	CAR-T	Lentiviral	Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL), diffuse large B-cell lymphoma (DLBCL)/ standard approval	Relapsed or refractory B-cell pre-cursor acute lymphoblastic leuke-mia (ALL), large B-cell lymphoma (LBCL), follicular lymphoma (FL) / standard Approval
Yescarta®	Axicabtagene ciloleucel	CAR-T	Retroviral	Relapsed or refractory dif-fuse large B-cell lymphoma (DLBCL) and primary medi-astinal large B-cell lymphoma (PMBCL)/standard approval	Relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, follicular lym-phoma (FL)/standard approval
Zynteglo®	Betibeglogene autotemcel	Gene addition	Lentiviral	Transfusion-dependent beta-thalassemia (TDT)/conditional approval	No longer marketed in the United States
Libmeldy® Lenmeldy®	Atidarsagene autotemcel	Gene addition	Lentiviral	Metachromatic leukodystrophy (MLD)/conditional approval	Metachromatic leukodystrophy (MLD)/standard approval
Tecartus®	Brexucabtagene autoleucel	CAR-T	Retroviral	Relapsed or refractory mantle cell lymphoma (MCL), Relapsed or refractory B-cell precursor acute lymphoblas-tic leukemia (ALL)/standard approval	Relapsed or refractory mantle cell lymphoma (MCL), Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)/ standard approval
Breyanzi®	Lisocabtagene maraleucel	CAR-T	Lentiviral	Relapsed or refractory dif-fuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma (HGBCL), primary mediastinal large B-cell lymphoma (PMBCL), and follicular lymphoma grade 3B/ standard approval	Relapsed or refractory large B-cell lymphoma (LBCL) after two or more lines of systemic therapy, follicular lymphoma (FL)/standard approval
Abecma®	Idecabtagene vicleucel	CAR-T	Lentiviral	Relapsed and refractory multiple myeloma/standard approval	Relapsed and refractory multiple myeloma/standard approval
Skysona®	Elivaldogene autotemcel	Gene addition	Lentiviral	Cerebral adrenoleukodystrophy (CALD)/conditional approval	Cerebral adrenoleukodystrophy (CALD)/standard approval
Carvykti®	Ciltacabtagene autoleucel	CAR-T	Lentiviral	Relapsed and refractory multiple myeloma/standard approval	Relapsed and refractory multiple myeloma/standard approval
Casgevy®	Exagamglogene autotemcel	Genome editing (CRISPR-Cas9)	N/A	Severe sickle cell disease and transfusion-dependent beta-thalassemia (TDT)/conditional approval	Severe sickle cell disease/standard approval
Lyfgenia®	Lovotibeglogene autotemcel	Gene addition	Lentiviral	No EMA approved indication	Sickle cell disease/standard approval

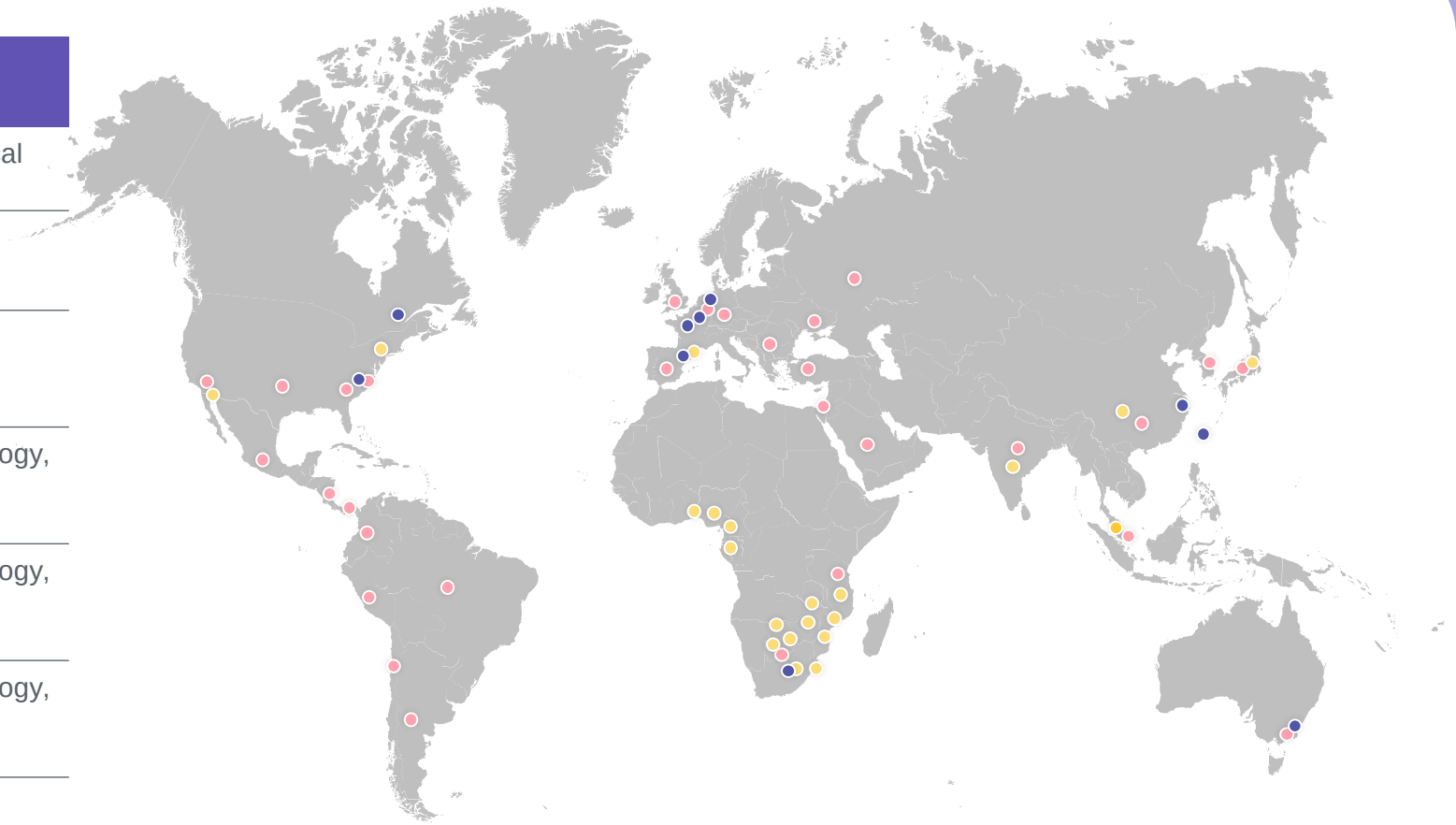
Ref: Carolina Iglesias-Lopez[1] · Antonio Vallano[2,3,4] · Antònia Agustí[2,5] Outlook of Cell Gene Therapies Development and Approval from Quality and Regulatory Perspective. *Therapeutic Innovation & Regulatory Science (2026) 60:823–836* https://doi.org/10.1007/s43441-026-00920-4

Delivering Global Solutions with Extended Laboratory Network

Local operations for efficiency and risk mitigation

Cerba Research

Region	Expertise
Belgium	Routine, Molecular Biology, Bioanalytical Lab, Flow Cytometry, Microbiology
The Netherlands	BSL3, Pre-clinical, Molecular Biology, Genetics/NGS, Pathology, Virology
France	Genetics/NGS, Molecular Biology, IVD, Flow Cytometry, Histopathology/ IHC, Virology, Biorepository, BSL3
North America (Montreal and NY)	Routine, Genetics/NGS, Molecular Biology, IVD, Flow Cytometry, Bioanalytical Lab/PK, Histopathology/IHC, Virology
China (Shanghai)	Routine, Genetics/NGS, Molecular Biology, Flow Cytometry, Bioanalytical Lab/PK, Histopathology/IHC
South Africa (Johannesburg)	Routine, Genetics/NGS, Molecular Biology, Virology, Microbiology, BSL3, Biorepository
Australia (Sydney)	Routine, Molecular Biology, Flow Cytometry, Virology



- Specialty Laboratories
- Pre-Processing Laboratories
- Research & Partner Laboratories

Flow Cytometry Laboratory Hubs

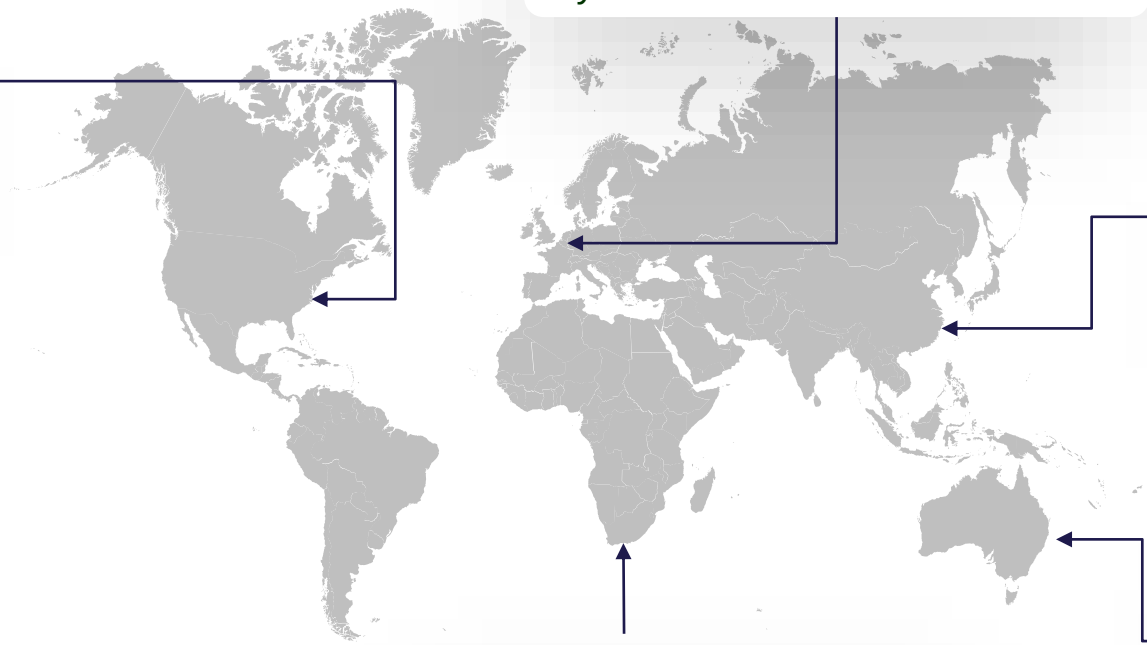
Delivering a Global Solution with Cerba Research's Extended Network

Cerba Research

US (New York)
CAP/CLIA/NYS
BD FACS Lyric
Cytek Aurora*

Belgium (Ghent)
ISO15189 (BELAC) & CAP/CLIA
BD FACS Lyric
Cytek Aurora*

China (Shanghai)**
ISO15189 (CNAS) & CAP
BD FACS Lyric
Cytek Aurora*





BD FACSLyric™: 3-laser conventional Flow cytometry



South Africa
ISO15189
BD FACSCanto II

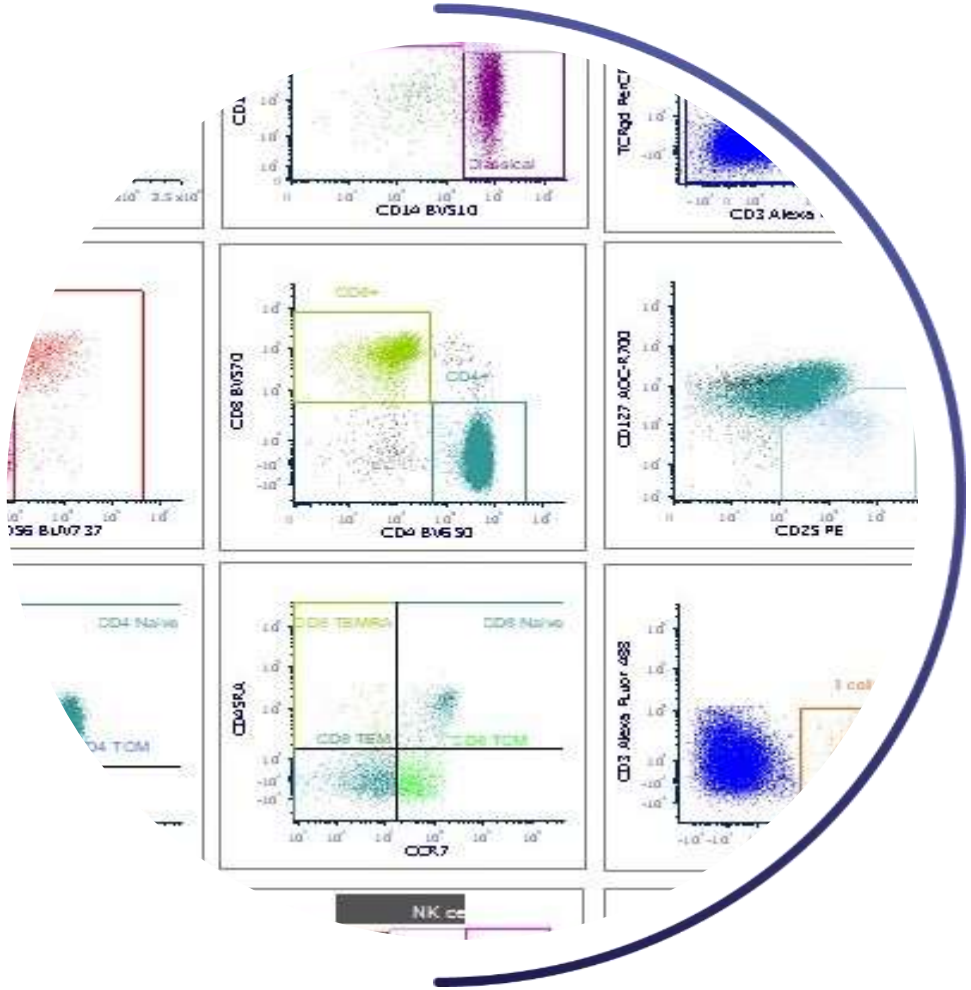
Australia (Sydney)
ISO15189 (SANAS)
BD FACS Lyric
Cytek Aurora*

AGILEX BIOLABS

**Cytek® Aurora: 5-laser Spectral Flow cytometry*

Customization: Choose from an array of assays as appropriate to your study

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Areas of Expertise

- Monitor immunophenotyping and cell activation
- Evaluate receptor occupancy of a drug
- Monitor and characterize CAR-T cells
- Detect intracellular cytokine production via intracellular staining (ICS) production.

Different matrices are used to validate the assays, including fresh and cryopreserved PBMC, blood and bone marrow aspirate.

Flow Cytometry Panels for CAR-T Therapy

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CART Enumeration panel: Basic T cell markers and CAR detection antibody. Includes quantitation of CAR expression and absolute counts

Fluorochrome	V500	PE	PerCP-Cy5.5	PE-Cy7	AF700	APC-H7
(Filter)	(528/45)	(586/42)	(700/54)	(783/56)	(720/30)	(783/56)
Tube 1 (FMO)	CD45	buffer	CD3	CD4	Viability	CD8
Tube 2 (FS)	CD45	CAR	CD3	CD4	Viability	CD8
Tube 3 (CAR quantitation)		Quantibrite				
Tube 4 (Trucount)	CD45					

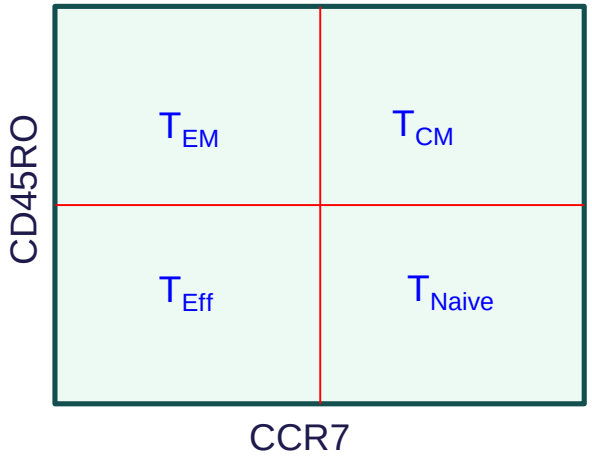


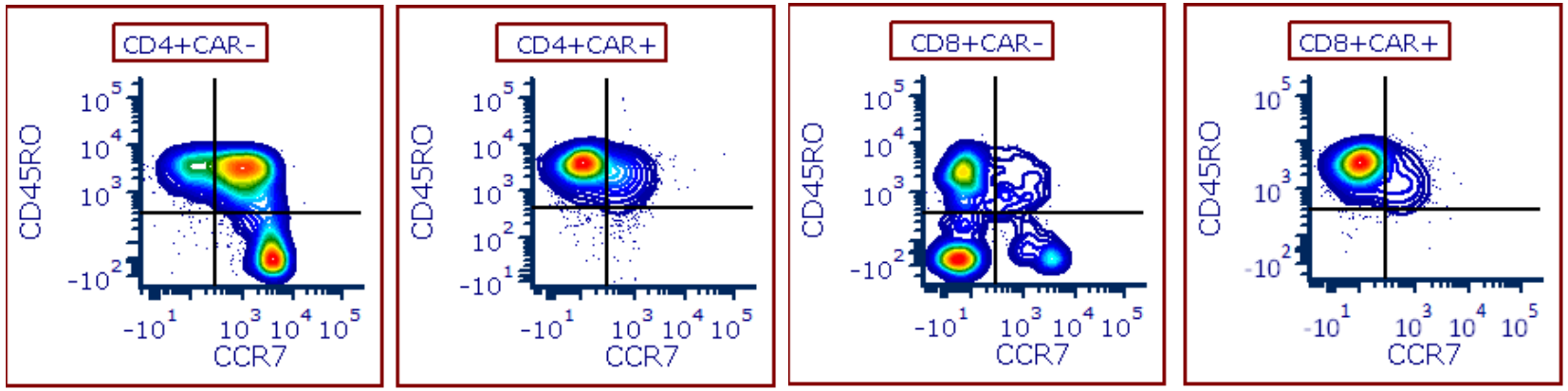
BD FACSLyric™: 3-laser conventional Flow cytometry

CAR-T Immunophenotyping Panel

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CART Characterization/immunophenotyping panel: T cell activation/exhaustion markers and memory subsets, and Treg cells for endogenous T cells and CART cells





✓ It is critical to understand the differentiation of CAR+ T cells into distinct memory subsets, as variation in these subsets influences the effectiveness of CAR+ T-cell therapy across individual patients.

Validated Flow Cytometry Panel Examples
BD FACSLyric™

Cerba Research

Panel Name*	Antigen Markers	Matrix	Sites
TBNK T cells, B cell, NK cells (relative % and absolute count)	**Tube 1:** CD3, CD4, CD8, CD16/CD56, CD19, CD45	Blood, BMA	US, EU, AUS, CHN
T cell NK panel T cell subsets (memory), gamma/delta T cells, NK cells (includes Ki67 marker)	Tube 1: CD3, CD4, CD8, (CD14 and Viability), CD16, CD45, CD56, Granzyme B, ICOS, Ki-67, PD-1, TCRγδ Tube 2: **CD3, CD4, CD8, (CD14 and Viability), CD25, CD45, CD45RA, CCR7, FoxP3, Granzyme B, Ki-67, PD-1** (includes Trucount tube for absolute count calculation)	Blood	US, EU, AUS
PBMC IC panel (intracellular cytokine assay)	**Tube 1:** CD3, CD4, CD8, CD45, CD183, CD194, IL-2, IL-4, IL-6, IFNγ, TNFα, viability.	PBMC	US
T cell NK panel T cell subsets (memory), gamma/delta T cells, NK cells (includes Ki67 marker)	**Tube 1:** CD3, CD4, CD8, (CD14 and Viability), CD16, CD45, CD56, Granzyme B, ICOS, Ki-67, PD-1, TCRγδ **Tube 2:** CD3, CD4, CD8, (CD14 and Viability), CD25, CD45, CD45RA, CCR7, FoxP3, Granzyme B, Ki-67, PD-1 (includes Trucount tube for absolute count calculation)	Blood	US, EU, AUS

*These are off the shelf-panels. The majority of panels that Cerba Research implements are proprietary to client programs.

Tracking Killer vs. Bystander Cell Dynamics

Utility of a validated TBNK panel

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Features/Population	What It Identifies	Insights on "Killer" vs. "Bystander" Effects
Effector/Killer Population	CD3+ CD8+ (T-cell therapy) or CD3- CD16+ CD56+ (NK therapy)	**Expansion and Persistence:** Quantifies the precise absolute count and percentage of the therapeutic "killer" cells over time to monitor their expansion post-infusion.
Endogenous Bystander T Cells	CD3+ CD4+ (Helpers) or native CD3+ CD8+	**Host Immune Reconstitution & Recruitment:** Shows if bystander T cells are expanding in response to cytokines (like IL-2 or IL-6) released during target killing, indicating an indirect cascade.
Bystander B Cells	CD3- CD19+ or CD20+	**Off-Target/Collateral Depletion:** In therapies like anti-CD19 CAR-T, B cells serve as a marker for the "killer" cell efficacy and off-target bystander aplasia (bystander B-cell elimination).
Bystander NK Cells	CD3- CD16+ CD56+ (when tracking T-cell therapy)	**Innate Immune Activation:** Measures if the patient's native NK cells are being recruited or enhanced by the local microenvironment to assist in tumor clearing.

Validated Spectral Flow Cytometry Panel Examples: Cytek Aurora

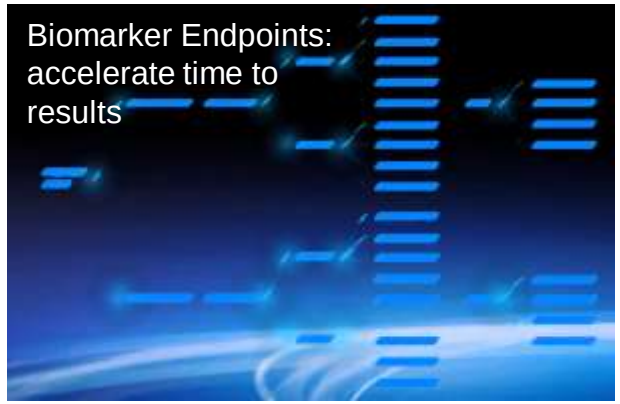
Cerba Research

Panel Name*	Antigen Markers	Matrix	Sites
TBNKM (14-colors, T cells, B cells, NK cells and monocytes, and subsets)	**Tube 1:** CD3, CD4, CD8, CD14, CD16, CD19, CD25, CD27, CD45, CD56, CD127, CD45RA, CCR7, IgD, Viability	PBMC, Blood	US, EU
TBNKM DC (25-colors, T cells, B cells, NK cells, monocytes and DC, and subsets)	**Tube 1:** CD1c, CD3, CD4, CD8, CD11c, CD14, CD16, CD19, CD20, CD25, CD27, CD28, CD38, CD45, CD45RA, CD56, CD123, CD127, CD141, CCR7, HLA-DR, IgD, IgM, PD-1, TCRγδ	Blood	US, EU
Pan immune profiling spectral flow cytometry assay (PIP-01)	**Tube 1:** (48-marker panel) (Markers lists on subsequent slide)	PBMC	US (Q3 2026)

*These are off the shelf-panels. The majority of panels that Cerba Research implements are proprietary to client programs.

Spectral Flow global footprint and Ozette partnership

High-Parameter Panel Data Analysis | Automated platform





Spectral Flow High-Parameter Power: Measure 40+ markers in a single panel for deep immune profiling and rare cell detection across oncology, immunology, and cell therapy.

Improved Sensitivity: Advanced optics and spectral unmixing improve detection of low-abundance markers and rare populations (e.g., MRD, Tregs).

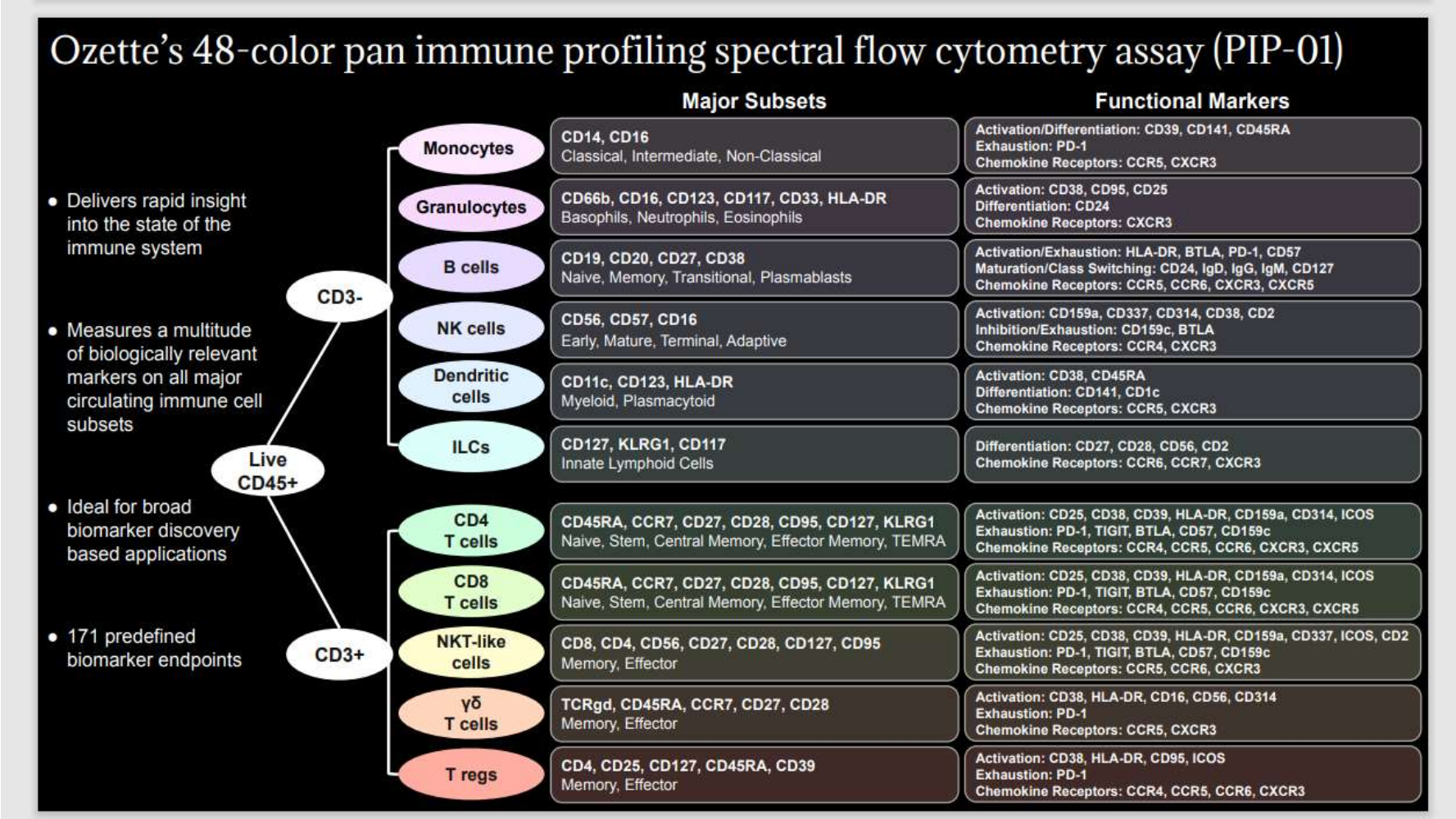
EndPoints Advanced Analytics: Rich spectral data supports machine learning, biomarker discovery, and multi-omic integration.

Ozette 48-Marker Spectral Reference Panel (PIP-01)

- Optimized 48-marker immune phenotyping panel for spectral flow
- Standardized backbone for discovery, translational, and early clinical studies
- Broad coverage of innate and adaptive immune lineages, including rare subsets
- Designed to maximize resolution while minimizing spectral spillover
- Enables consistent population definitions across multi-site and multi-sponsor studies

Cerba Research Data In-house; MRD=minimal residual disease

Ozette's 48-color pan immune profiling spectral flow cytometry assay (PIP-01)



Conclusion

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High-Dimensional Immunophenotyping in a Single Tube

Tracking the interplay between therapeutic cells and bystanders requires an immense number of markers. Spectral flow allows for panels exceeding **40+ colors simultaneously**, enabling you to capture a complete profile of both populations at once:

- **Killer/Therapeutic Lineage:** Target antigens, CAR/TCR expression, and exhaustion markers (e.g., PD-1, TIM-3, LAG-3)
- **Bystander Architecture:** Endogenous CD4+ / CD8+ T cells, regulatory T cells (Tregs), NK cells, and myeloid-derived suppressor cells (MDSCs).
- **Functional State:** Cytokine production (IFN-γ, TNF-α), proliferation (Ki-67), and cytotoxic molecules (Granzyme B, Perforin) across both groups.

Scaling it globally: From single site to global clinical trials

Cerba Research

Implementing complex characterization strategies across global trials introduces operational and scientific challenges that must be solved deliberately, not left to chance.

01



Assay standardization

Harmonized protocols and reference materials so results are comparable across every testing site.

02



Data integration

Unified data structures that connect flow, genomic, and BioA outputs into one interpretable dataset.

03



Global deployment

Coordinated logistics, training, and lab networks to maintain consistency across regions.

04



Consistency and scalability

Quality systems that hold up as programs scale from early-phase to global pivotal trials.

Thank you

For more information, contact:

Kirsty Maclean
kmaclean@cerbaresearch.com

Cerba Research



cerbaresearch.com