



Enabling Cytokine Therapeutic Development with Qualified, Functional Cell-Based Assays

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OUR EXPERTISE
IN YOUR HANDS.
DISCOVER
CONFIDENTLY.

Eurofins DiscoverX Is a Global Leader in Cell-Based Assays for Screening, Profiling, Potency & Lot Release Programs



DiscoverX

The Eurofins Discovery PRODUCTS COMPANY

From Discovery to Development to Clinic to Post-Market

20+ Years Experience Building Cell-Based Assays



San Francisco Bay Area, California

R&D & Manufacturing:
San Francisco Bay Area, California (HQ)
St. Charles, Missouri
Poitiers, France

10+ Druggable
target
classes

**Industry's Largest
Cell Based Assay
Portfolio**

1500+
Stable cell lines and
Membrane Preps

>30 Billion
Data Points Screened

**ICH-based
Pre-Qualified
Bioassays**

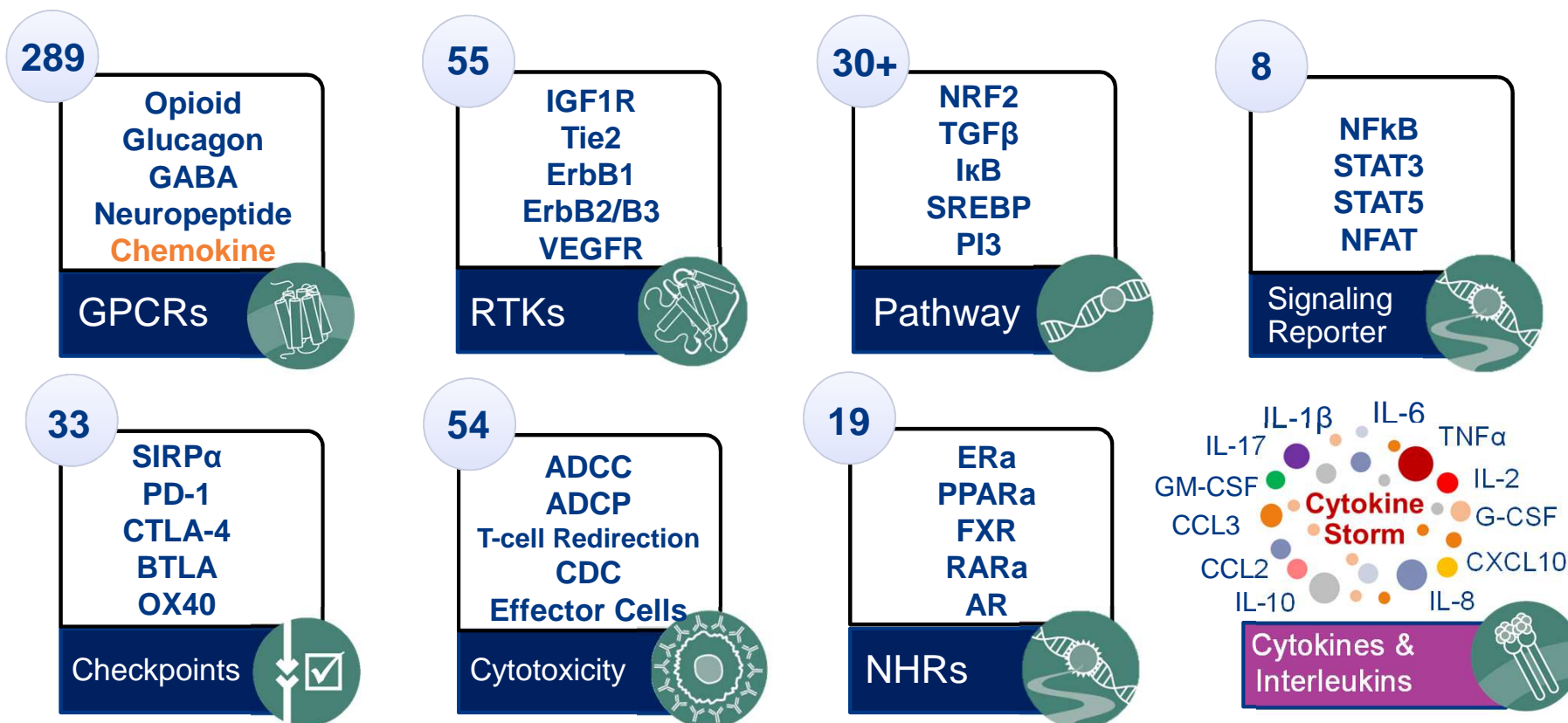
**End-to-End
Method Transfer
Support**

4 Certified
CRO
Partners


**Supporting 70+
Global Programs**
For potency, stability and NAb testing

Largest Menu of Cell-Based Assays for Discovery, Potency & NAb Assay Development

>1500+ Cell Lines and Membrane Preps to support bioassay development for major drug target classes

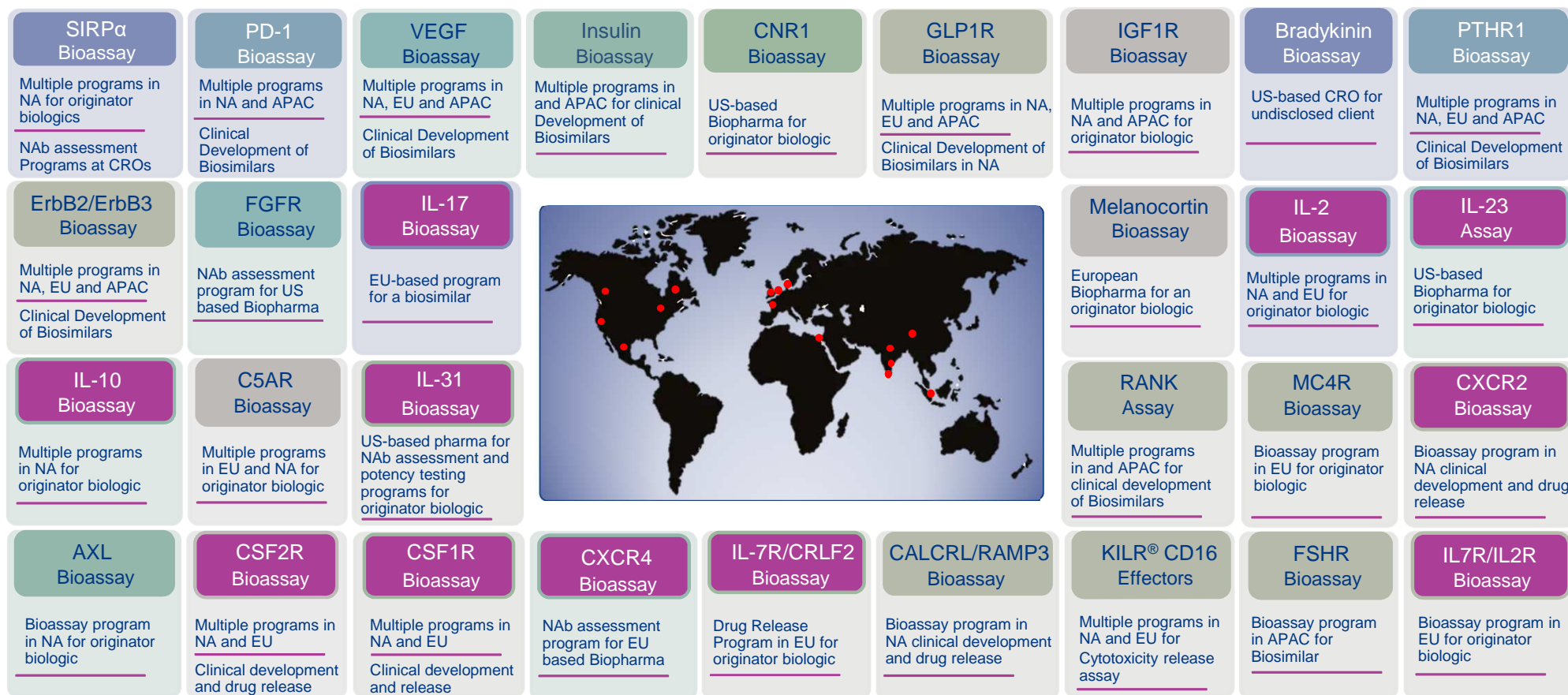


Global Programs using DiscoverX Bioassays for Potency, Stability & NAb Testing for Drug Release

SIRPα Bioassay Multiple programs in NA for originator biologics NAb assessment Programs at CROs	PD-1 Bioassay Multiple programs in NA and APAC Clinical Development of Biosimilars	VEGF Bioassay Multiple programs in NA, EU and APAC Clinical Development of Biosimilars	Insulin Bioassay Multiple programs in and APAC for clinical Development of Biosimilars	CNR1 Bioassay US-based Biopharma for originator biologic	GLP1R Bioassay Multiple programs in NA, EU and APAC Clinical Development of Biosimilars in NA	IGF1R Bioassay Multiple programs in NA and APAC for originator biologic	Bradykinin Bioassay US-based CRO for undisclosed client	PTHR1 Bioassay Multiple programs in NA, EU and APAC Clinical Development of Biosimilars
ErbB2/ErbB3 Bioassay Multiple programs in NA, EU and APAC Clinical Development of Biosimilars	FGFR Bioassay NAb assessment program for US based Biopharma	IL-17 Bioassay EU-based program for a biosimilar				Melanocortin Bioassay European Biopharma for an originator biologic	IL-2 Bioassay Multiple programs in NA and EU for originator biologic	IL-23 Assay US-based Biopharma for originator biologic
IL-10 Bioassay Multiple programs in NA for originator biologic	GM-CSF Bioassay Multiple programs in EU and NA for originator biologic	IL-31 Bioassay US-based pharma for NAb assessment and potency testing programs for originator biologic				RANK Assay Multiple programs in and APAC for clinical development of Biosimilars	MC4R Bioassay Bioassay program in EU for originator biologic	CXCR2 Bioassay Bioassay program in NA clinical development and drug release
AXL Bioassay Bioassay program in NA for originator biologic	CSF2R Bioassay Multiple programs in NA and EU Clinical development and drug release	CSF1R Bioassay Multiple programs in NA and EU Clinical development and release	CXCR4 Bioassay NAb assessment program for EU based Biopharma	IL-7R/CRLF2 Bioassay Drug Release Program in EU for originator biologic	CALCRL/RAMP3 Bioassay Bioassay program in NA clinical development and drug release	KILR® CD16 Effectors Multiple programs in NA and EU for Cytotoxicity release assay	FSHR Bioassay Bioassay program in APAC for Biosimilar	IL7R/IL2R Bioassay Bioassay program in EU for originator biologic

Key: NA = North America; EU = Europe; APAC = Asia Pacific; NAb = Neutralizing Antibody

Global Programs using DiscoverX Bioassays for Potency, Stability & NAb Testing for Drug Release

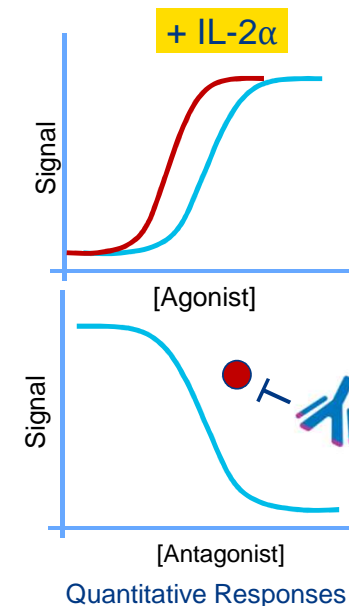
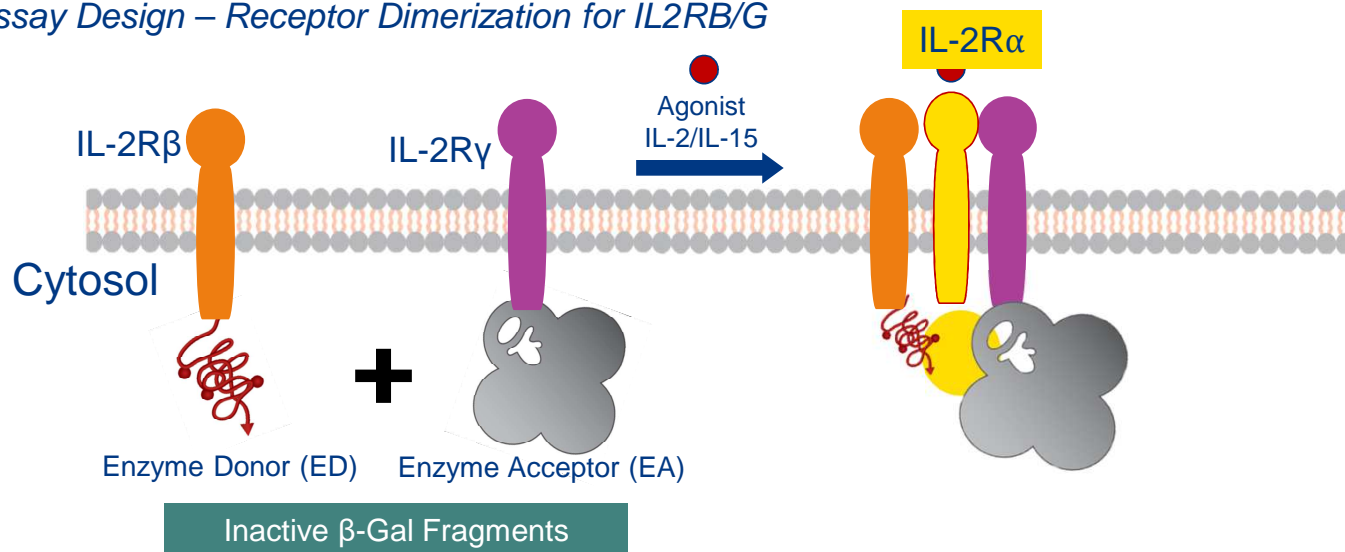


Key: NA = North America; EU = Europe; APAC = Asia Pacific; NAb = Neutralizing Antibody

Assay Design

Enzyme Fragment Complementation (EFC) Technology

Assay Design – Receptor Dimerization for IL2RB/G



Homogenous

- Add-and-read assay format
- No washing steps
- No centrifugation step
- No shaking or filtration

Robust

- Large signal-to-background
- Gain of signal assay design
- High assay accuracy, precision and reproducibility

Qualified and Validated

- ICH-Based Qualification
- Validated at GMP CRO
- Screened billions of data-points

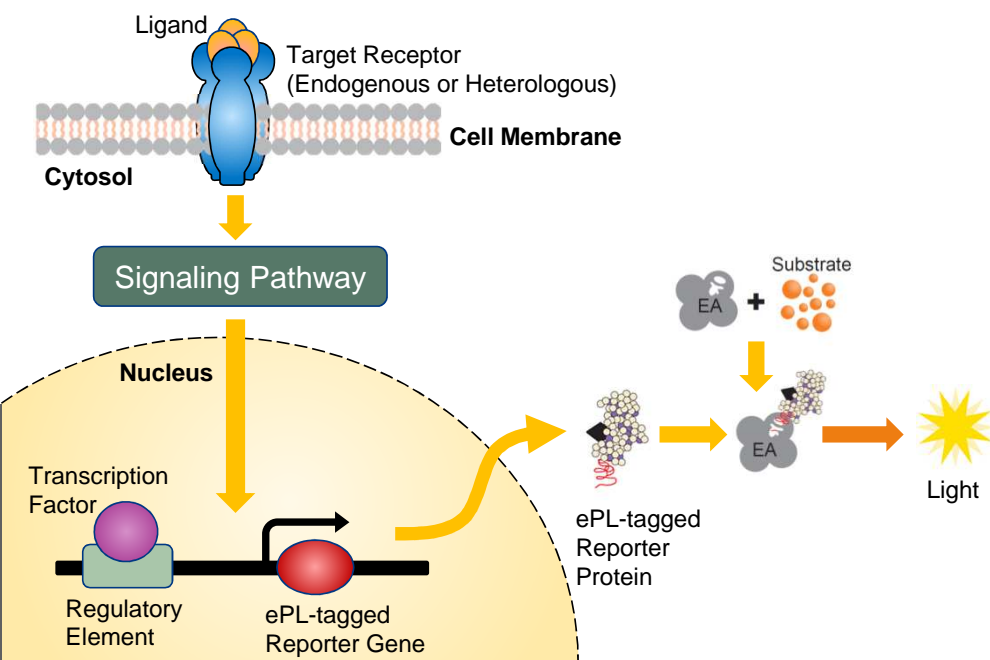
Easy to Transfer

- Assay protocol is similar across platform
- Detailed user manuals
- Method transfer support

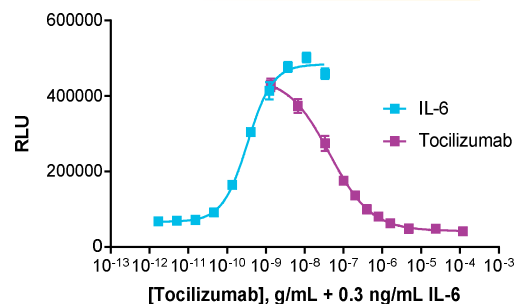
Signaling Pathway Reporter Assays for Cytokines

Signaling Reporter Pathway

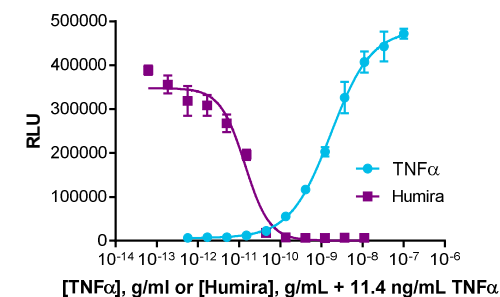
STAT3, STAT5, NF- κ B, NFAT,



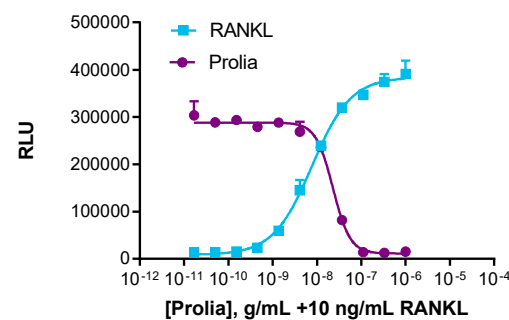
PathHunter® HepG2
STAT3 Pathway Reporter Assay



PathHunter U2OS
NF- κ B Pathway Reporter Assay



PathHunter U2OS RANK
NF- κ B Pathway Reporter Assay



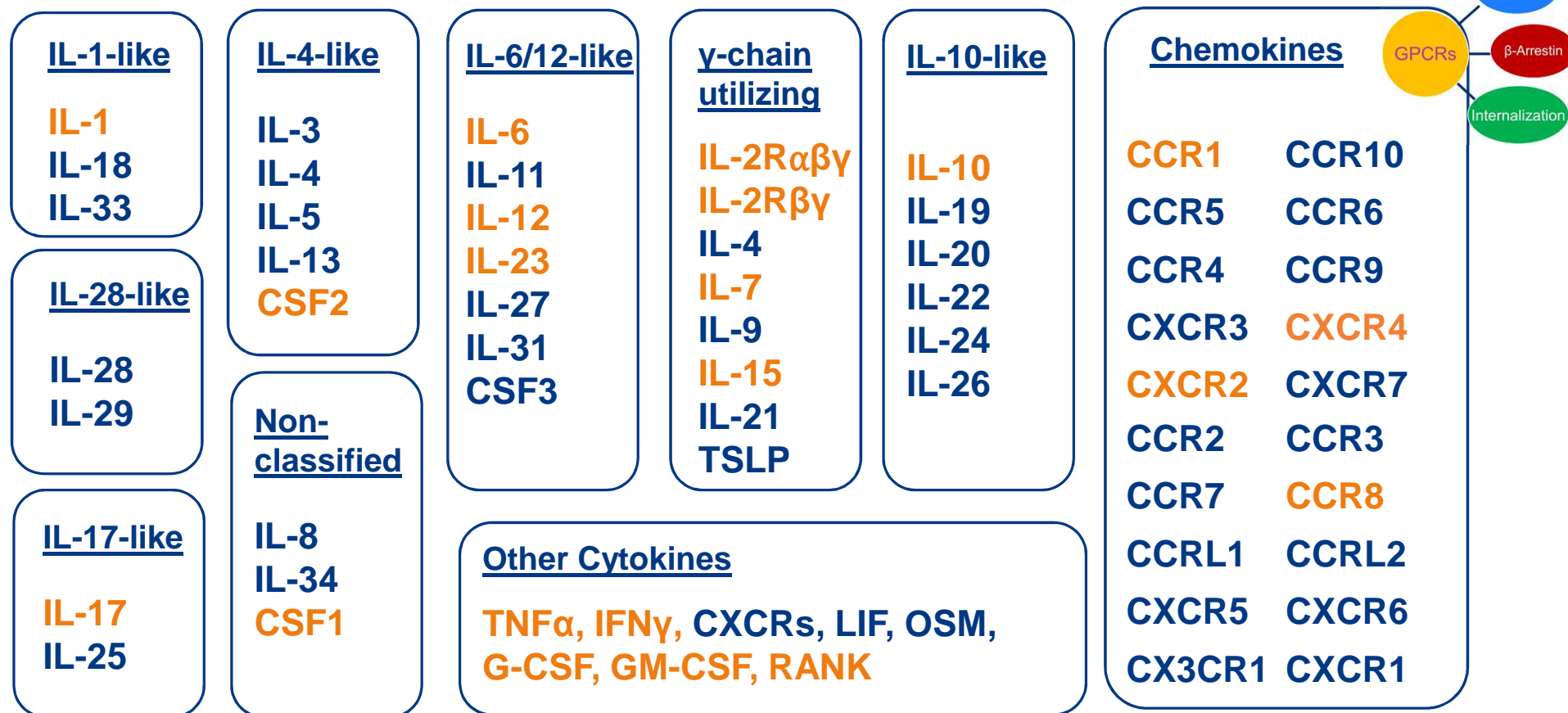
Cytokine Assay Portfolio



DiscoverX

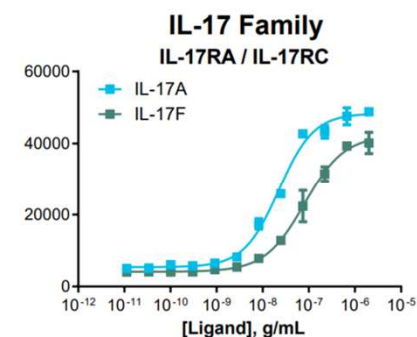
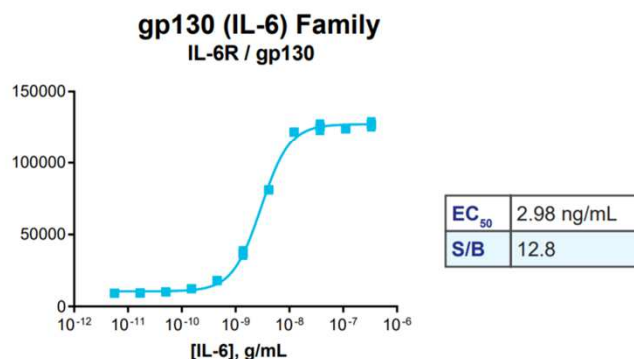
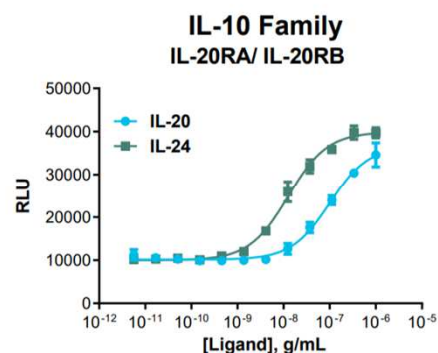
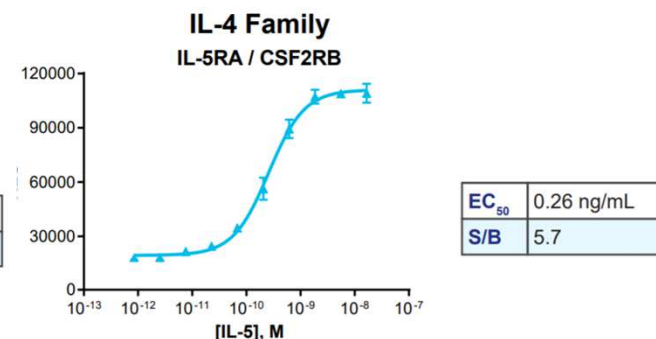
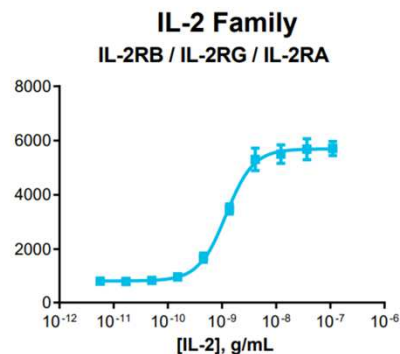
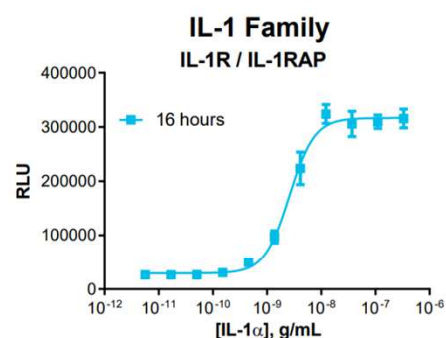
The Eurofins Discovery PRODUCTS COMPANY

Functional assays for >80% human interleukins and cytokines



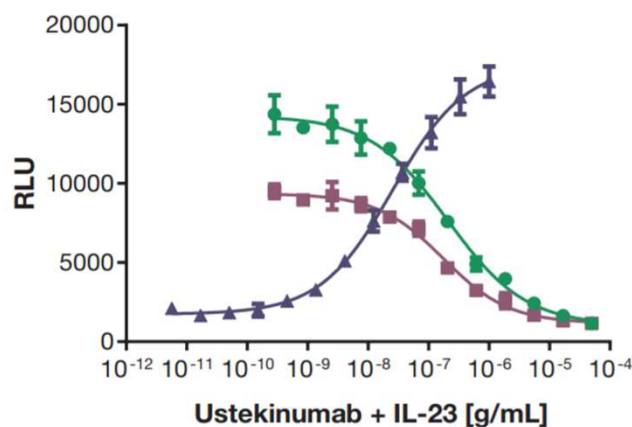
Highly Specific Assays for Interleukin Receptors Across Multiple Families

Robust assay windows and high reproducibility



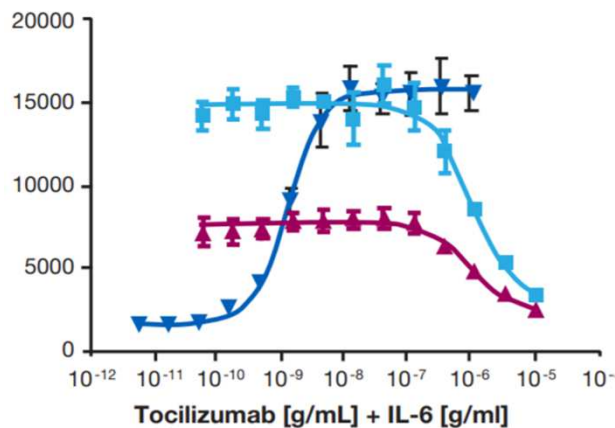
Functional Assays for Therapeutic Antibodies and Inhibitors for Interleukin Receptors

Ustekinumab (Stelara®)
IL-12RB1/IL-23R Assay



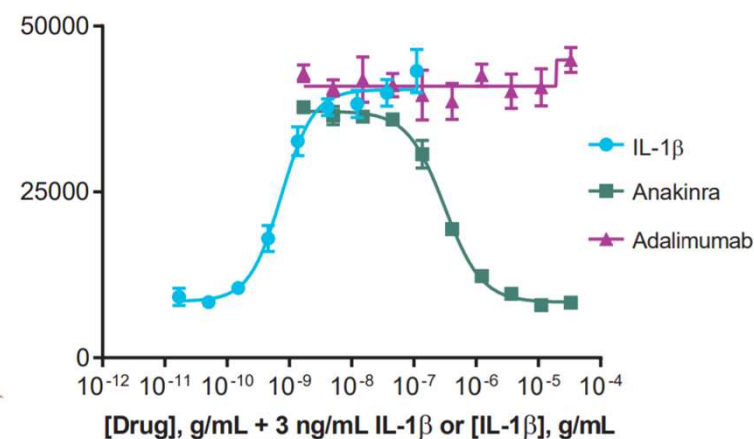
	EC ₅₀	S/B
● Ustekinumab +100ng/mL IL-23	2.096e-007	12.4
■ Ustekinumab +50mg/mL IL-23	1.750e-007	8.2
▲ IL-23	2.570e-008	9.9

Tocilizumab (Actemra®)
IL-6R/IL-6ST Assay



	IC ₅₀	S/B
■ Tocilizumab +3ng/mL IL-6	1.001e-006	4.8
▲ Tocilizumab +1ng/mL IL-6	9.591e-007	3.3
▼ IL-6	1.255e-009	9.9

Anakinra (Kineret®)
IL-1R/IL-1RAP Assay

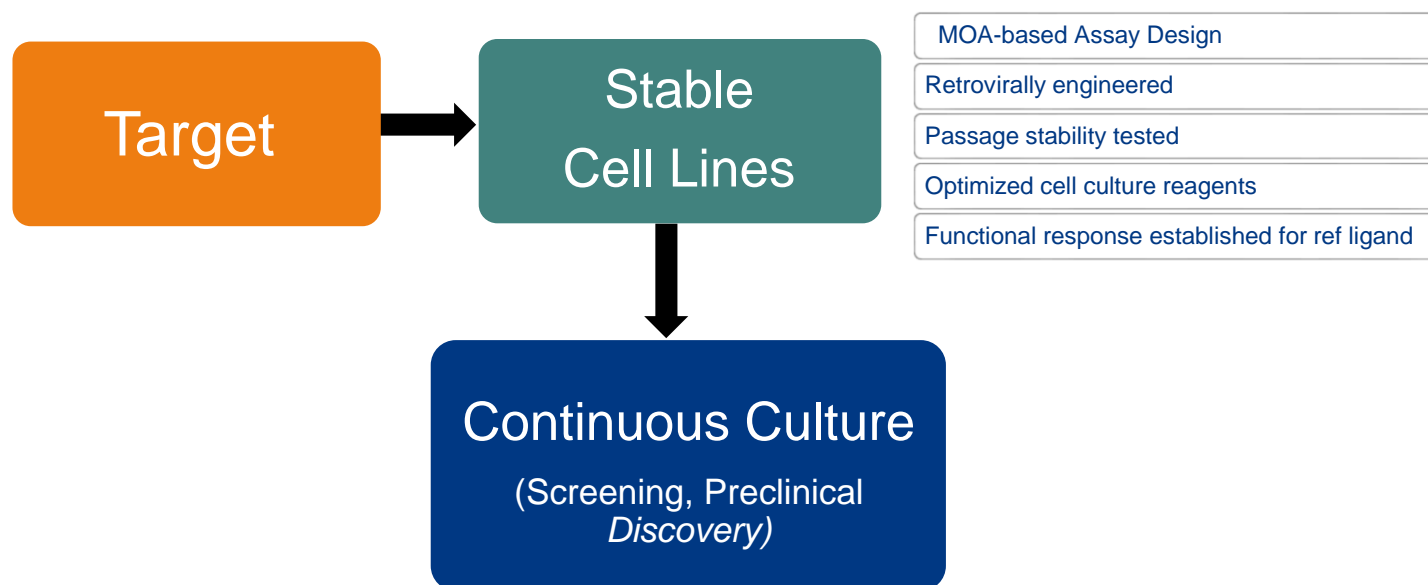


	IL-1β	Anakinra	Adalimumab
S/B	5.5	4.2	-
EC ₅₀ / IC ₅₀ (ng/mL)	0.84	302	-

Phase Appropriate Assay Formats

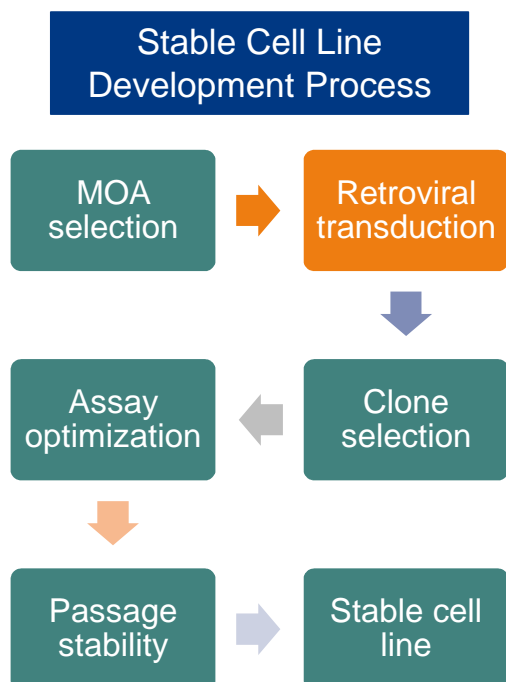
Bioassays Offer Phase-Appropriate Assay Formats for Every Development Program

From continuous culture to qualified Bioassays

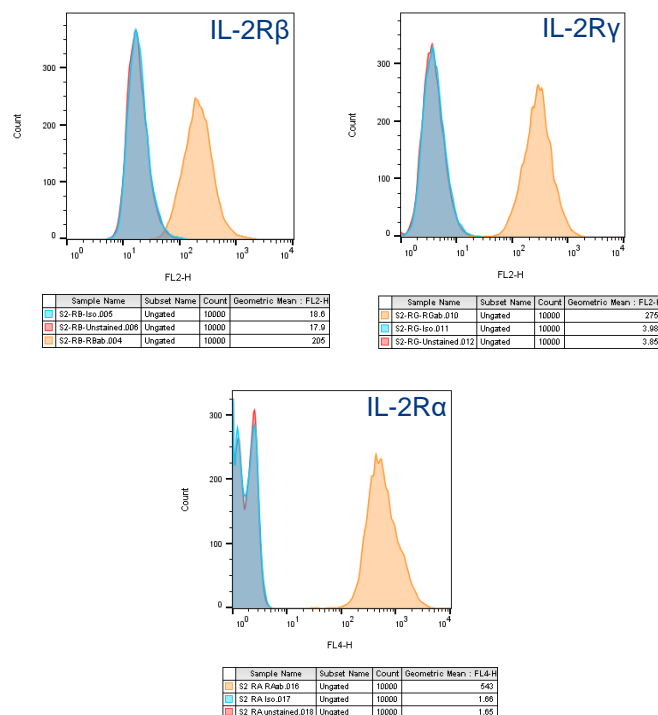


Stable Cell Line Generation

Stability of surface expression by flow cytometry compared to functional response

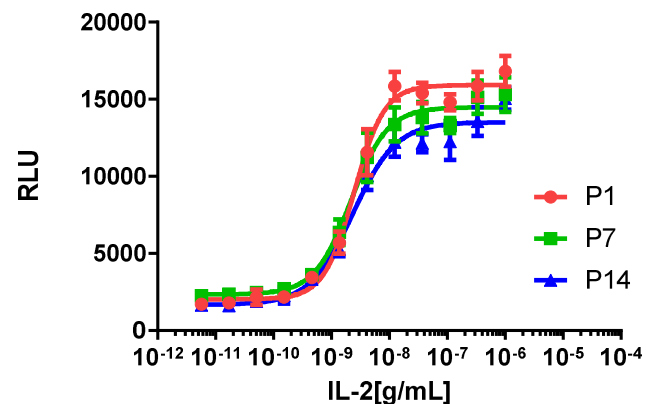


Surface Expression Assessed by Flow Cytometry



Functional Stability

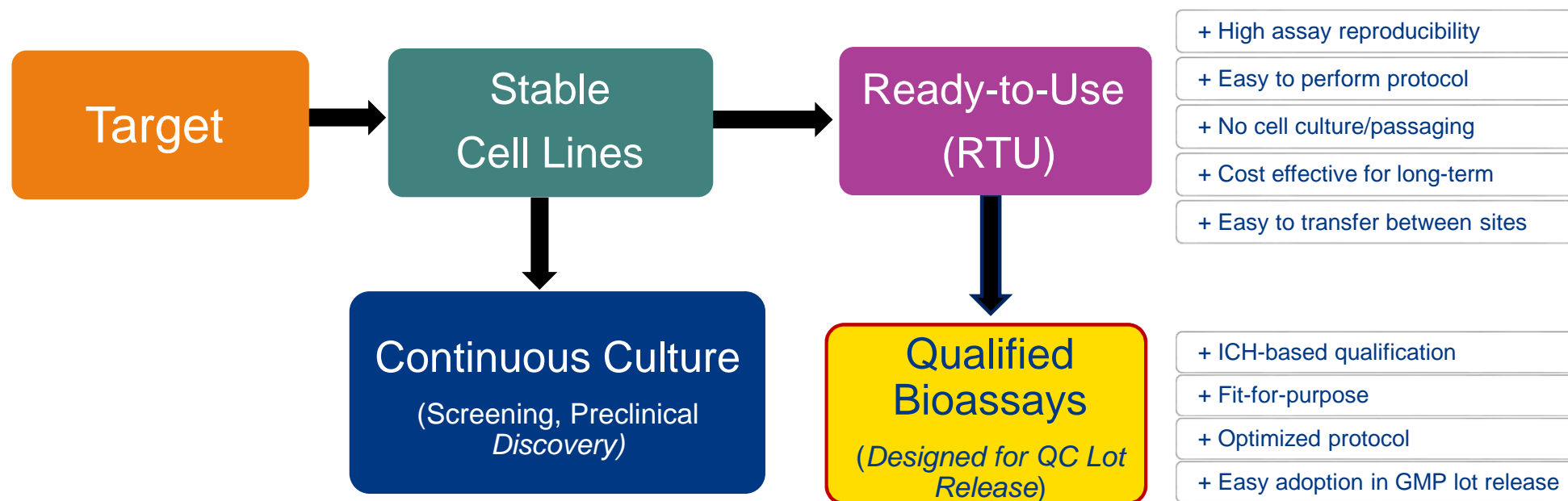
Passage Study Data



	P1	P7	P14
HillSlope	1.661	1.378	1.167
EC50	2.457e-009	2.162e-009	2.344e-009
S/B	9.8	6.7	9.1

Bioassays Offer Phase-Appropriate Assay Formats for Every Development Program

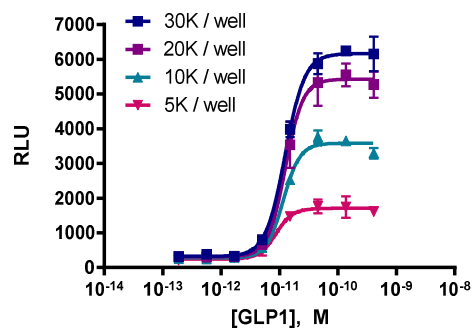
From continuous culture to qualified Bioassays



Focused Optimization for Deriving Ready-to-Use Bioassay Format

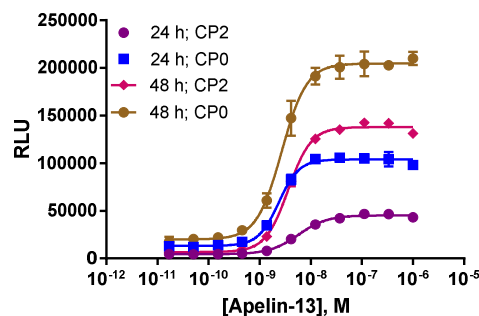
Examples of parameters evaluated for frozen ready-to-use cells

Cell Density Optimization



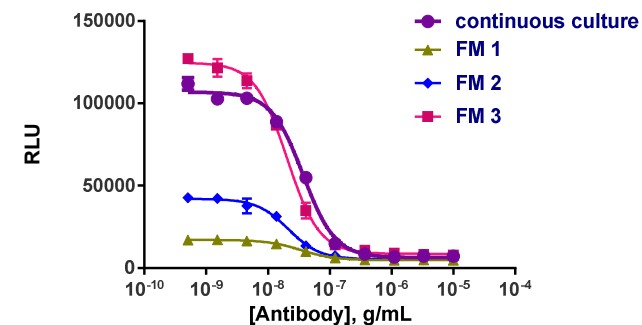
	30K/well	20K/well	10K/well	5K/well
EC ₅₀	1.23x10 ⁻¹¹	1.27x10 ⁻¹¹	1.1x10 ⁻¹¹	7.5x10 ⁻¹²
S/B	14.8	15.0	11.7	5.0

Recovery Time and Assay Medium



	24 h; CP2	24 h; CP0	48 h; CP2	48 h; CP0
EC ₅₀	5.7x10 ⁻⁹	2.35x10 ⁻⁹	3.63x10 ⁻⁹	2.97x10 ⁻⁹
S/B	10.9	10.2	22.8	11.9

Effect of Freezing Medium on Functional Response



	Continuous Culture	FM 1	FM 2	FM 3
IC ₅₀ (ng/mL)	37.1	39.9	21.3	20.4
S/B	16.9	3.9	8.0	14.5

Ligand Incubation Time

Detection Reagent Optimization

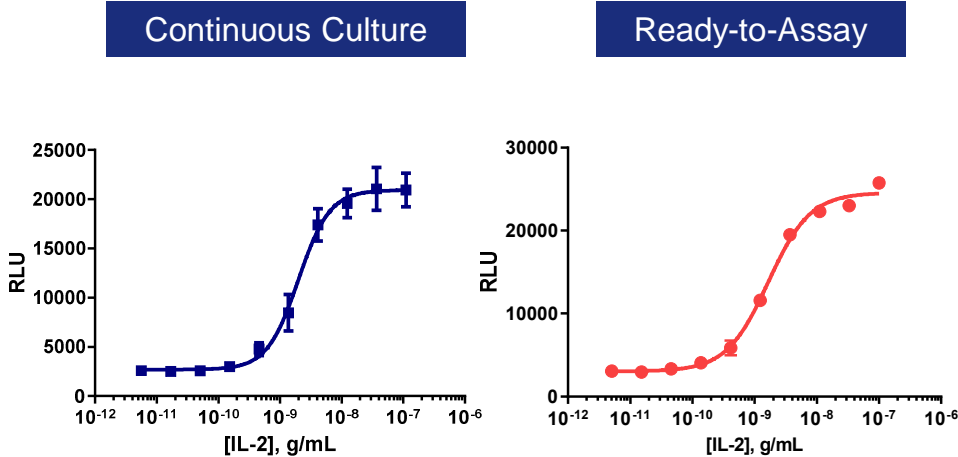
Ligand Incubation Temperature

Dilution Buffer Composition

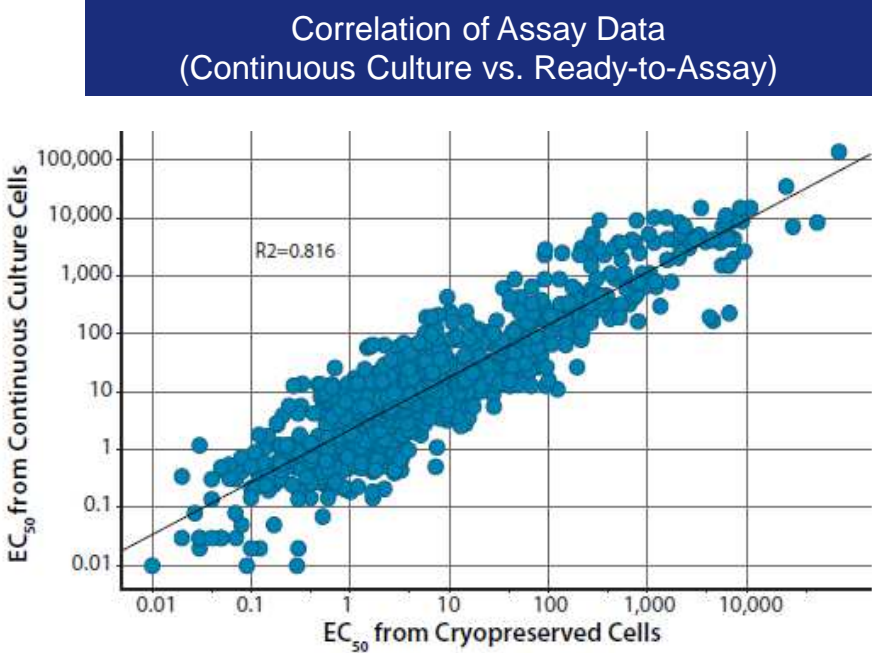
Matrix Sensitivity

Optimal Cell Number/Vial for Freezing

Excellent Concordance between EC₅₀: Continuous Culture vs. Ready-to-Assay Cell Formats



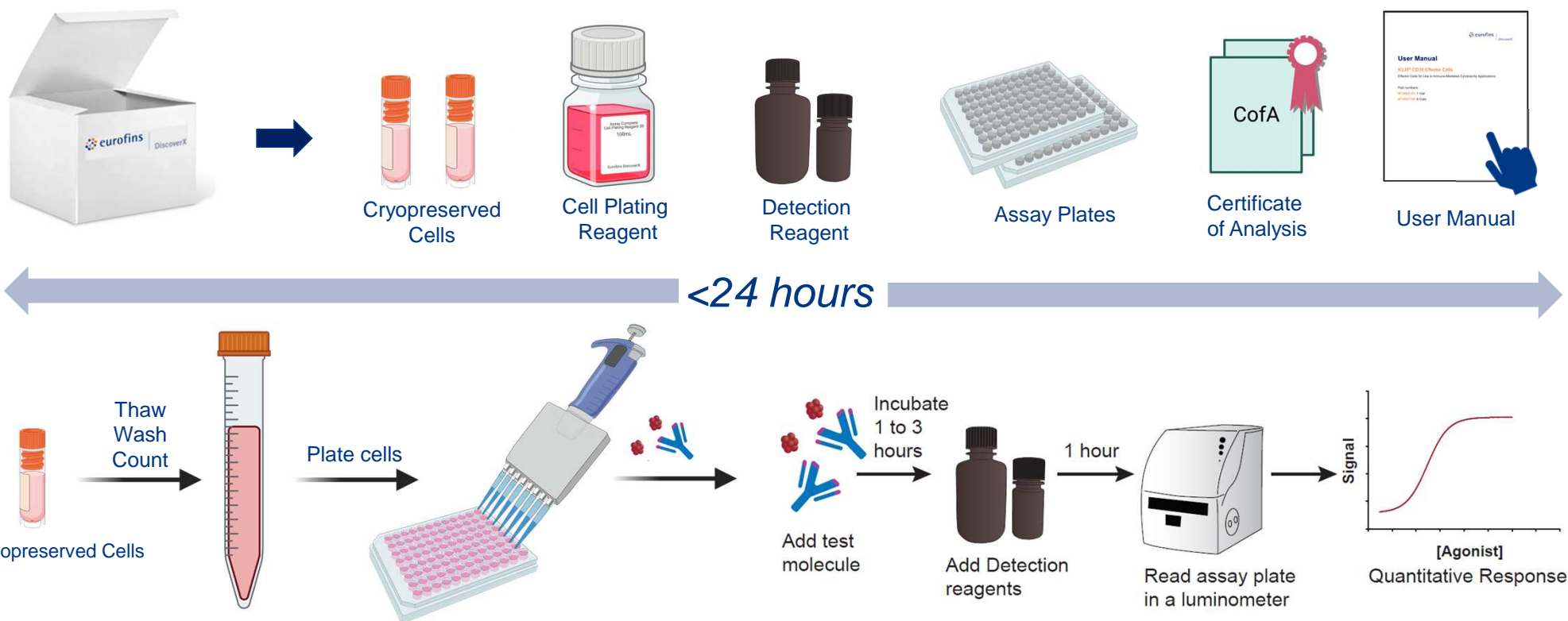
Format	Hill Slope	EC ₅₀ (ng/mL)	S/B
Cell Line	1.7	1.9	9.6
Bioassay	1.4	1.7	8.1



For overwhelming majority of targets assay performance matches closely between the stable cell line and ready-to-use assay cells

Bioassay Kit Includes all Key Components and Offers Easy-to-Use Assay Protocol

Bioassay Kit Includes Required Reagents for the Assay



Industry Requirements Drives Bioassay Development Strategy (Following ICH Guidelines)

- **Reflective of MOA of the drug/molecule**
- **Stability-indicating**
- Relative potency range (50%-150%)
- Repeatable, robust, precise, and accurate
- Reproducible
 - Intra-lot (plate-to-plate)
 - Inter-lot (lot-to-lot)
 - Analyst-to-analyst

Long-term support – Dedicated well characterized cell banks

Supply agreements

Traceability and quality (audit-ready)

ICH-based Assay Qualification

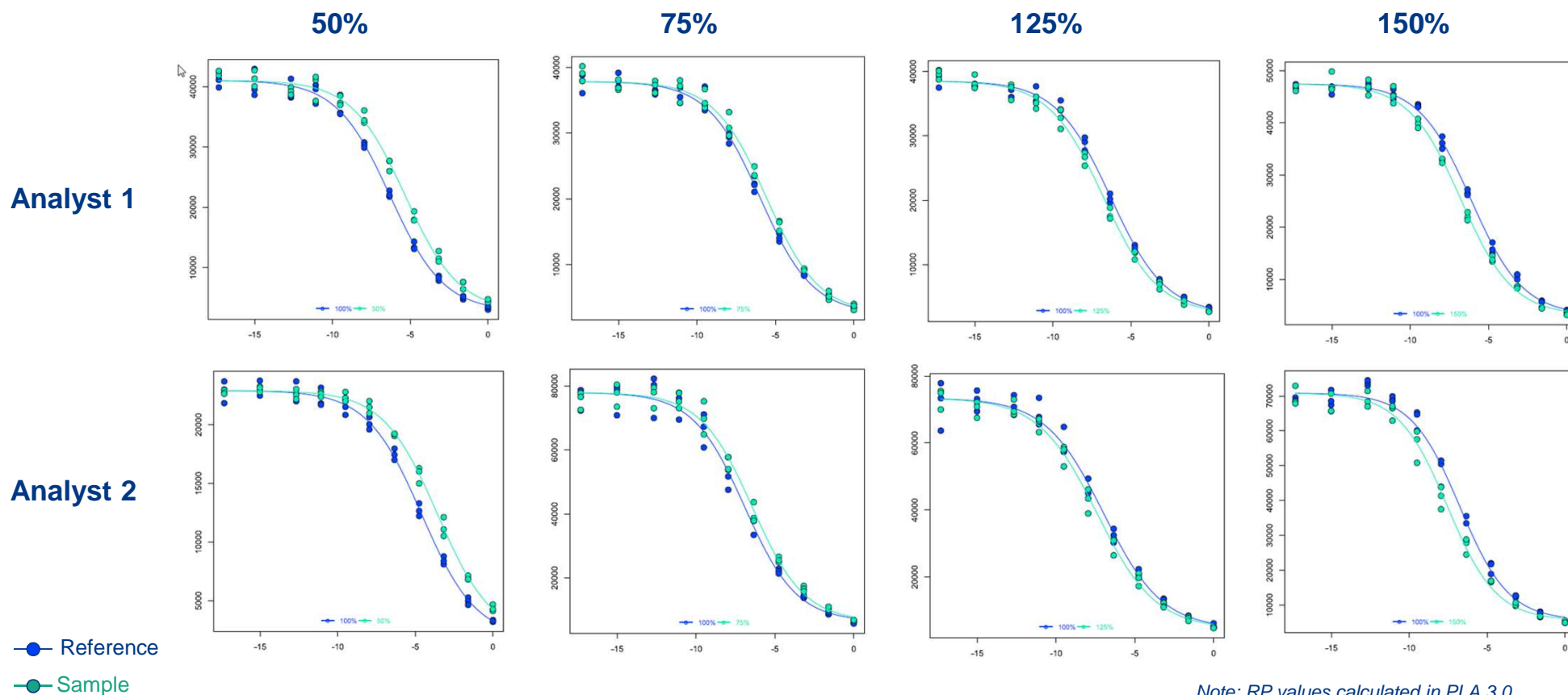


ICH = International Council for Harmonization

Parallelism and Relative Potency Estimation



Relative Potency: Parallelism and Potency Estimation (PLA)

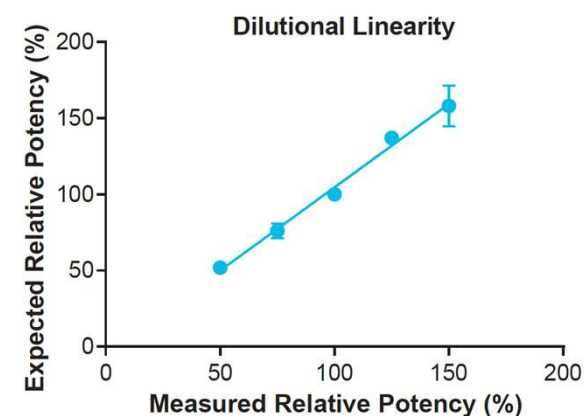


Tocilizumab Bioassay: Qualification with Actemra®



Summary: Accuracy, Precision and Dilutional Linearity (Single Analyst)

Experiment #	Analyst #	Expected RP (%)	Observed RP (%)	Average RP (%)	% RSD	% Recovery
1	1	150	155.5	158.1	8.44	105.4
2	1		163.2			
3	1		141.1			
4	2		172.7			
1	1	125	138.6	137.1	1.66	109.7
2	1		137.4			
3	1		138.6			
4	2		133.8			
1	1	75	74.1	76.1	6.34	101.5
2	1		83			
3	1		75.4			
4	2		71.9			
1	1	50	54.8	52	4.96	103.9
2	1		50.6			
3	1		53.3			
4	2		49.1			



Dilutional Linearity: 99.27%

Accuracy: 105.1%

Precision: 5.4%

Tocilizumab Bioassay is highly accurate, precise and linear!

Off-the-Shelf, Ready-to-Use Qualified Bioassays for Biologics and Biosimilars

 **ACTEMRA®**
tocilizumab

IL-6

 **EYLEA™**
aflibercept solution for injection

VEGF

 **KEYTRUDA**

PD-1

 **PERJETA®**
pertuzumab for injection

HER2

 **Aranesp®**
darbepoetin alfa injection

EPO

 **FORTÉO™**
teriparatide (rDNA origin) injection

PTH

 **Kineret®**
(anakinra)

IL-1

 **Vectibix®**
(panitumumab)
Injection for IV Infusion

EGFR

 **AVASTIN®**
bevacizumab
100 MG/4 ML INJECTION FOR IV USE

VEGF

 **GONAL-f®**
FOLLITROPIN ALFA

FSH

 **Leukine®**
sargramostim
A Recombinant GM-CSF-Yeast-Expressed

GM-CSF

 **VICTOZA®**
liraglutide injection 1.2 mg | 1.8 mg

GLP-1

 **Byetta®**
exenatide injection

GLP-1R

 **HGH** SOMATROPIN
Recombinant Human Growth

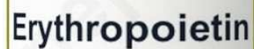
hGH

 **LUCENTIS®**
RANIBIZUMAB INJECTION

VEGF

 **HUMIRA**
adalimumab

TNFα

 **Erythropoietin**

EPO

 **Humalog®**
insulin lispro

Insulin

 **NovoLog®**
insulin aspart (rDNA origin) injection

Insulin

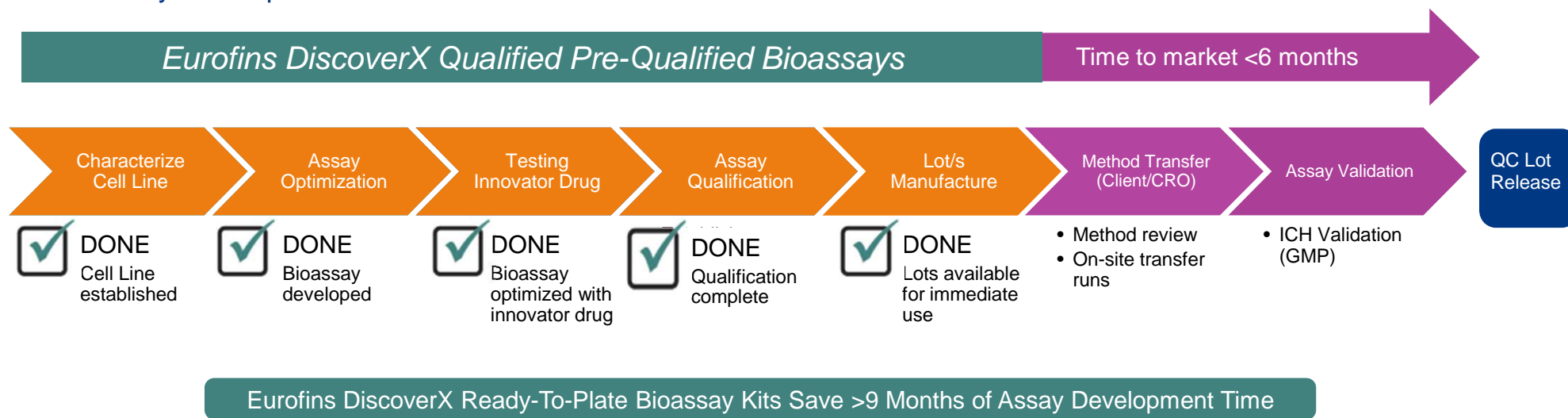
 **OPDIVO®**
(nivolumab)

PD-1

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Qualified Bioassays for Precise Potency Determination for Cytokines and Interleukins

Typical Bioassay Development Timeline



Strong Relationships with Global CROs



Eurofins Discovery Translational Phenotypic Services

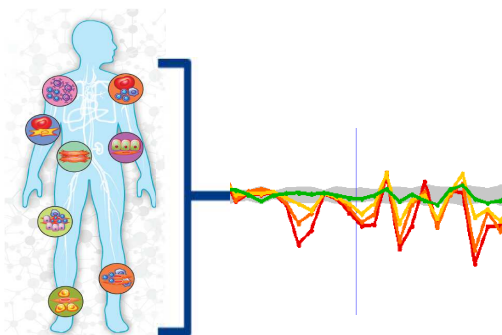
Translational Phenotypic Services Center of Excellence

Advancing client pipelines since 2000 with cell-based assays and analytics

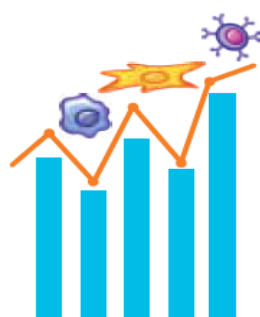


- Benefit from human data early in discovery
- Make sense of complex disease biology
- Reveal novel mechanisms-of-action
- Identify translational biomarkers
- Uncover drug resistance and safety risks

BioMAP® Platform Services



Biomarker Services



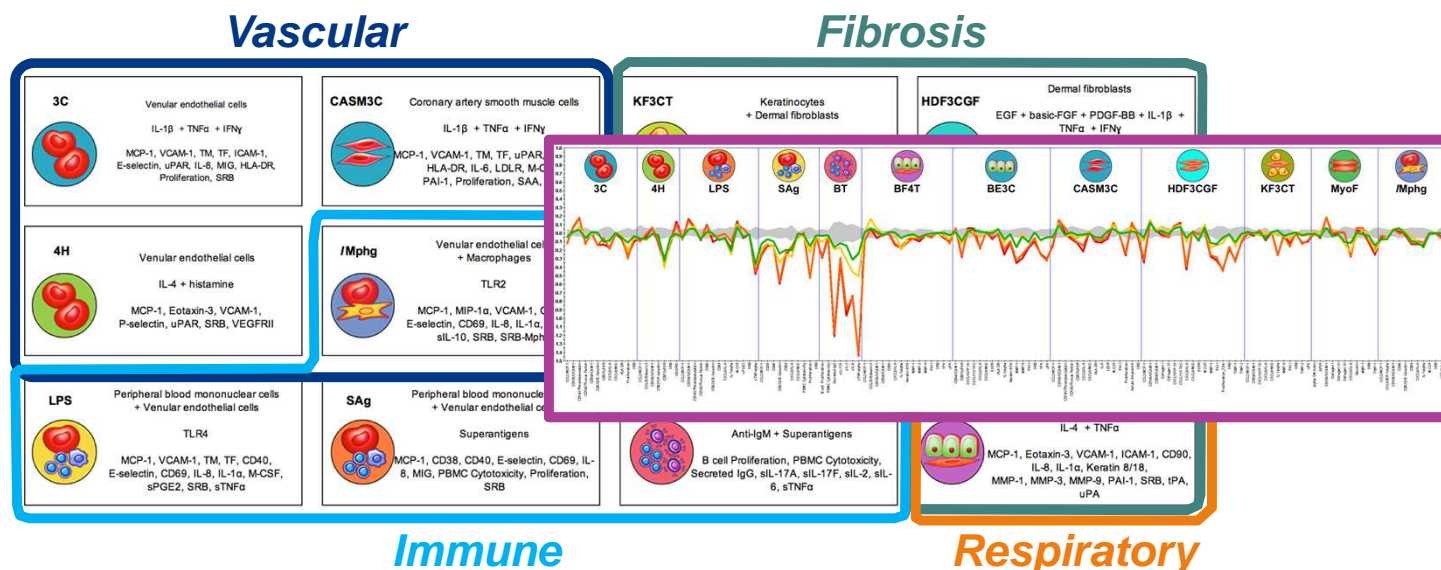
OncoPanel™ Services



Custom Services



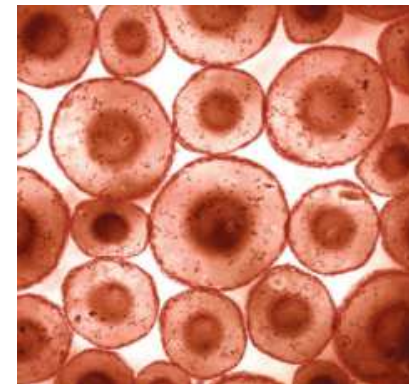
Platform Flagship Service: BioMAP® Diversity PLUS® Panel



- Human primary cell-based disease models collected into an assay panel
- Assays capture broad range of human biology: cell proliferation & DNA repair, vascular biology, immune biology
- Stimulation conditions model adaptive responses: inflammation, immune responses, tissue remodeling, wound healing

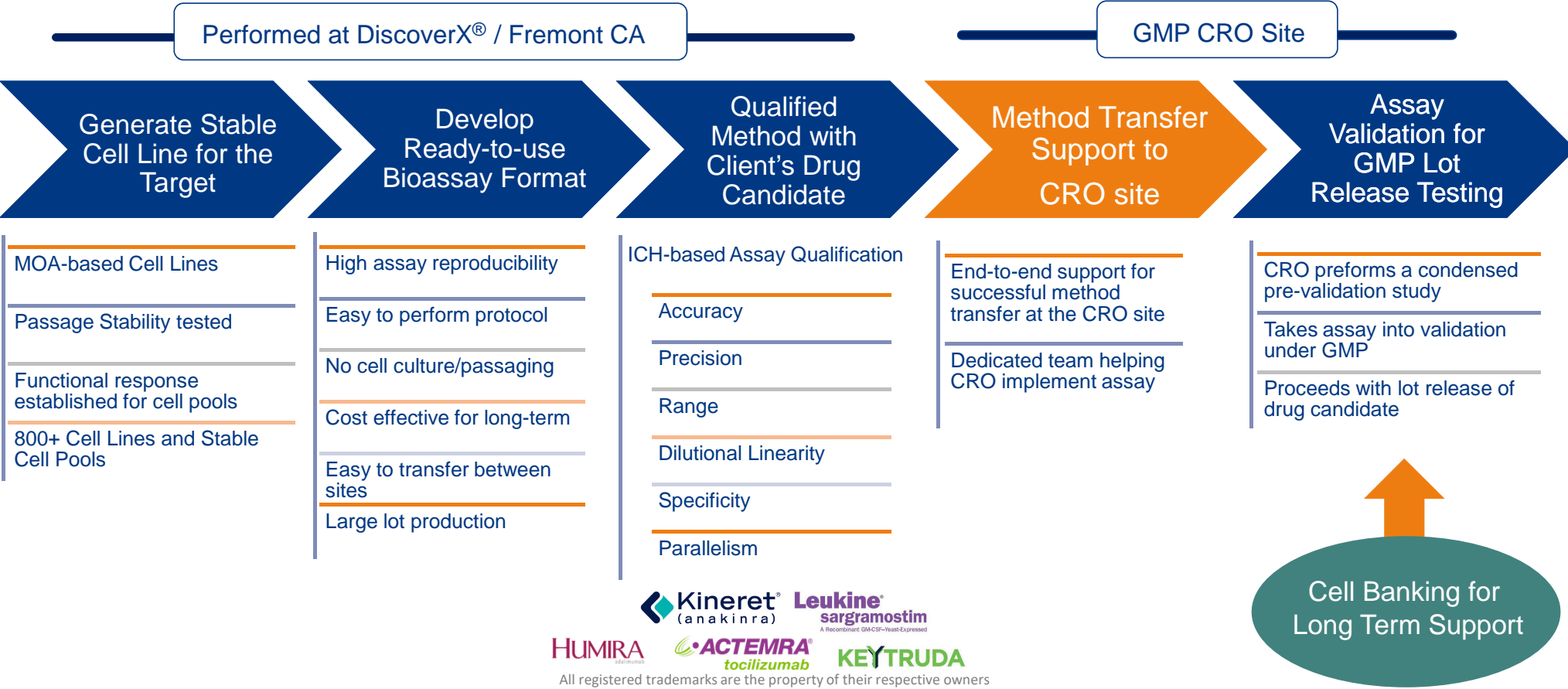
Cytokines and Beyond — Standard and Custom Assay Services

- Standard studies conducted with a unique bank of PBMCs from 13 different human donors
 - ✓ Male and female
 - ✓ Variety of ethnicities
 - ✓ Variety of ages
- Options to meet diverse client needs
 - ✓ Jurkat, THP-1, and other tumor cell lines (including Eurofins Discovery OncoPanel™ Collection)
 - ✓ HUVEC and other primary cell types
 - ✓ Mouse, rat, dog, pig, non-human primate (NHP) PBMCs, and other cell types
 - ✓ Custom cell types (e.g. engineered cell lines)
- Technology platforms are selected to best suit the specific client application
 - ✓ Luminex & Meso Scale Discovery platforms
 - ✓ ELISA
 - ✓ HTRF (homogeneous time resolved FRET)
 - ✓ Flow cytometry
 - ✓ High-content imaging
 - ✓ Mass spectrometry



www.eurofinsdiscoveryservices.com

Custom Assay Development, ICH-Based Qualification and Method Transfer Support for QC Lot Release to GMP CRO



Summary



DiscoverX® offers the industry's largest menu of cell-based assays, with over 1,500 off-the-shelf products

PathHunter® Cytokine and Interleukin Assays platform offer MOA-based Dimerization and Signaling Reporter assays covering over 80% of targets

Qualified Ready-to-use Bioassays significantly accelerate potency and stability testing for quality control lot release programs for cytokines and interleukins

Through cytokine, chemokine, membrane receptor, and cell health biomarker readouts, the BioMAP® platform provides preclinical human data on MOA, efficacy and safety

Come visit us at our booth!

Drug Discovery & Development Phase-Appropriate Solutions | Our Expertise in Your Hands – Discover Confidently

Visit discoverx.com/interleukin to learn more

