Building a Technology Toolkit to Support the Emerging Science Landscape

Dr. Julie Frearson
Corporate Vice President, Strategic Alliances

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Market Trends

C&GT pipeline growing and with pricing main challenge

- After 20 years of R&D, first approvals of genuine gene therapies occurred last year (Luxturna for retinal dystrophy by Spark; Zolgensma for SMA by Novartis)
- Pipeline of such therapies is substantial; main challenge is minimal effective dose understanding and pricing ($425K per eye or $2.1M for SMA drug)
- FDA expects to approve between 10 to 20 C&GT drugs per year by 2025 based on an assessment of the current pipeline and the clinical success rates of these products

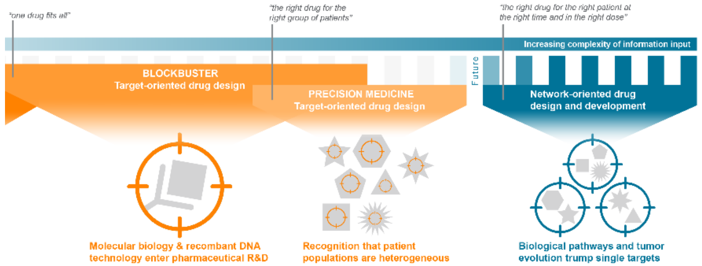
AI having real world impact

- 96% success rate in adenoma detection via polyps by applying artificial intelligence (AI) to images from colonoscopies (typical ADR 7-53%)
- Enterprise AI deployments are beginning to reach commercial scale
- Global Enterprise AI software, hardware, and services revenue reached $23.6B in 2018

Dementia disease: Starting all over again

- Long line of clinical trial failures in the Alzheimer's space
- From 1998 to 2017, nearly 150 failed attempts at developing Alzheimer's drugs, and 2018 marked another half-dozen or so failures
- March 2019 - Biogen Eisai failure finally closed the door on the beta amyloid hypothesis

Gaining interest in applying precision medicine throughout DSA

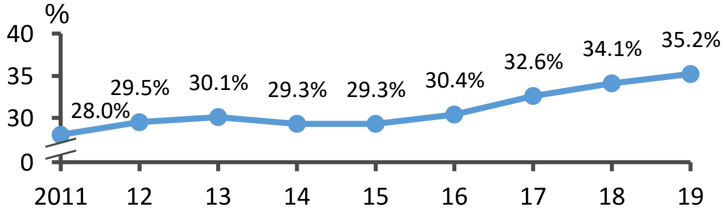


Super-sized funding environment

- Series A and IPOs have been fewer in number, but much larger ($80-100M Series A and $300-600M IPOs)
- Investments happening earlier driven by confidence in C&GT and increasing number of platforms that can spread investment across multiple TAs
- Super-sized series A and IPOs correlate into biotech investing in the best teams and aiming to go to market without M&A or asset sales

Oncology continues to dominate TAs

Percent of pipeline in development for cancer (2011-2019)



Source: Citeline

Significant developments in R&D: Cell & Gene Therapy (C&GT) revolution, digitalization of science, and funding concentrations

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Technology Partnerships

- Partnerships are a driving force behind our strategy and future growth
  - Risk-mitigated partnerships address strategic **portfolio gaps** and **drive revenue growth** with a lower upfront commitment from CRL
    - Supplement organic growth and our M&A strategy
  - Offer ability to thoroughly **test the technology and market opportunity** before a potential acquisition
- Focus of partnering activities
  - Driving differentiation via technologies which **enhance speed to develop a clinical candidate** and **make earlier go/no-go decisions** (i.e. fail drugs faster)
- Success metrics for our partnership strategy
  - Goal to have 5-8 partnerships at steady state, accretive during partnership
  - Pre-negotiated terms for potential M&A to ease process and onboarding
  - Focus on **alignment of incentives to provide win-win** for CRL and partner

SCIENCE TREND #1: Therapeutic choices

Small Molecule	Antibody / Protein (enzyme, peptide, CRISPR)	Cell therapy	Gene therapy
Accessible market: ~$5B **CAGR: 7%**	**Accessible market: ~$1.8B** **CAGR: 10-17%**	**Accessible market: ~$0.7B** **CAGR: 30%**	**Accessible market: ~$0.7B** **CAGR: 30%**

Ease of administration; Low cost of goods; Lower chance of clinical POC

Specificity; High cost

Precision; Higher chance of clinical POC; Safety considerations; Speed to market

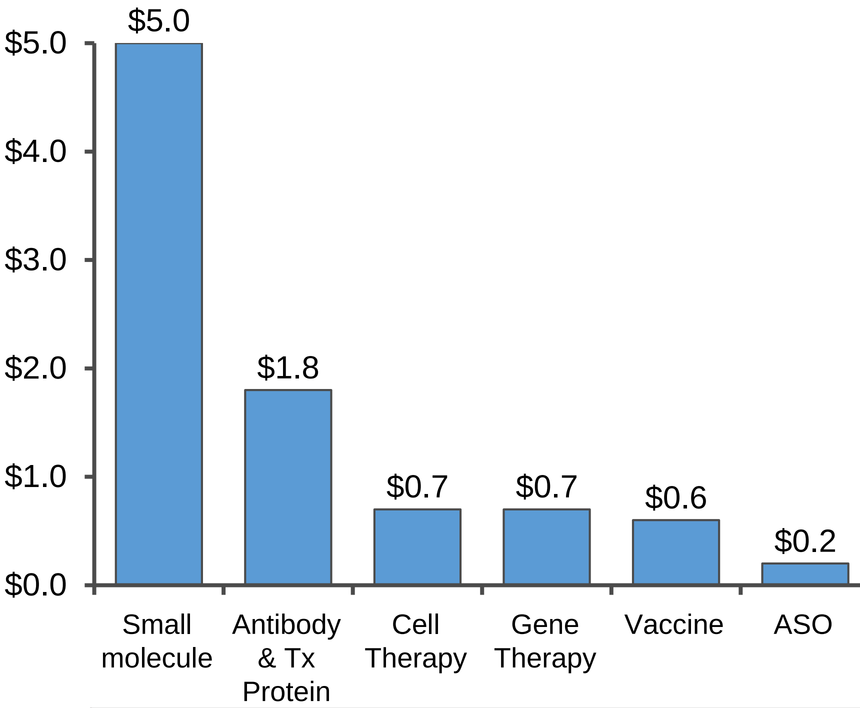
The nature of drug development has changed dramatically: Our clients have a multitude of options with many drugs from new modalities being approved

Source: Citeline and CRL management estimates

Significant Opportunity in Biologics

- Pipelines and FDA approvals are increasing significantly for biologic drugs, particularly in C&GT
- CRL Safety Assessment (SA) revenue is currently derived from ~60% small molecule drugs and ~40% biologics
  - Mix shift anticipated due to strong growth in C&GT
  - Believe C&GT drugs could represent ~25% of the pipeline over time
- Small molecules will remain largest area of drug research
  - Market is more mature with expectation for moderate growth
- Antibody therapeutics have become “mainstream,” but a strong growth opportunity remains
  - Opportunity for incremental growth by enhancing large molecule discovery capabilities via next generation approaches
- C&GT is rapidly emerging as a precision option with a rapid path to clinic and validation by recent market approvals
  - CRL is already a leading C&GT CRO, particularly for Safety Assessment capabilities
  - Additional opportunities exist to further participate through market and technology adjacencies

DSA Market Opportunity by Modality (2018)
(US$ in billions)



Projected Market CAGR Through 2024 (%)					
7%	12%	30%-35%	30%-35%	3%	10%

Source: Citeline and CRL management estimates

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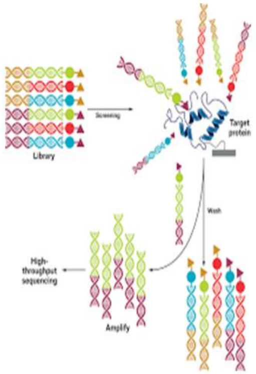
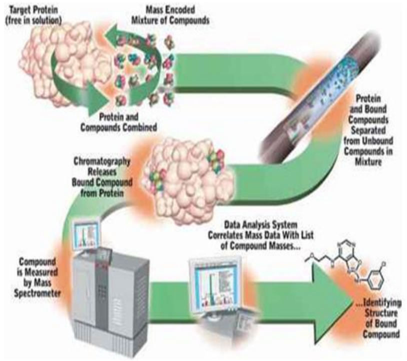
Small Molecule Technologies

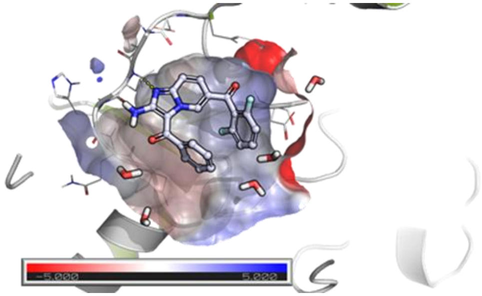
- DSA has a comprehensive portfolio of small molecule capabilities
- Focused on enhancing productivity of small molecule drug discovery efforts
  - Extending what is currently druggable; Reduce time and cost
- Partnerships aimed to strengthen:
  - Diverse & unbiased chemical libraries/screening platforms
  - *In silico* predictive technologies (AI)
  - Next-generation structural elucidation of targets
  - Improved target ID technologies



DNA encoded library platform



Unbiased binding mass spec

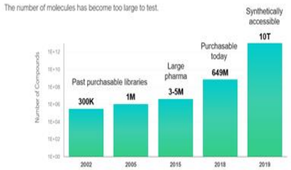


AI-enabled virtual screening

Huge diversity

Huge diversity & Speed

Binds to any available site on target (unbiased)



Extreme diversity and unbiased binding tackles previously "undruggable" targets

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Novel Antibody Technologies

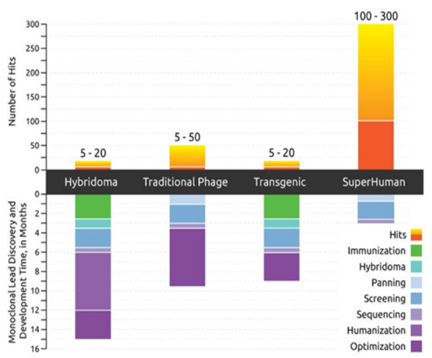
- CRL SA is well positioned to help clients develop novel antibody therapies
  - Study value and complexity is higher than with small molecules
- *In vivo* Discovery (pharmacology) is also well positioned in this modality
- Emerging platforms to discover new antibodies in Early Discovery
  - Evaluating next-generation antibody and CAR-T reagent platforms to support advanced discovery efforts
  - Distributed Bio partnership performing well

Diversity
- 76 billion antibodies
- >5000 enriched, specific clones against every target panned
- Picomolar hits against each antigen
- Unprecedented, fully-natural CDR diversity
- Computationally optimized CDR fitness

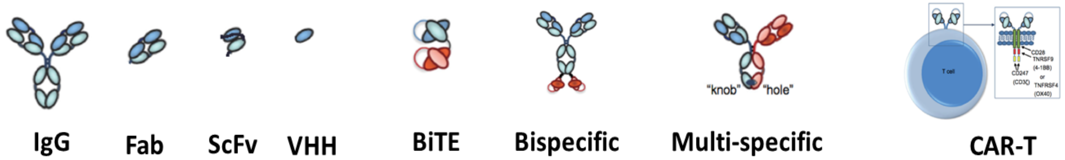
Developability
- Drug-worthy scaffolds
- Naturally selected CDR diversity
- 100% germline frameworks
- Enhanced thermostability
- Depleted liabilities

Speed
- Single-pass multi-parameter optimization
- Easy affinity maturation
- Easy cross-species optimization
- Agile vector system

Development time / number of hits:



Example antibodies:



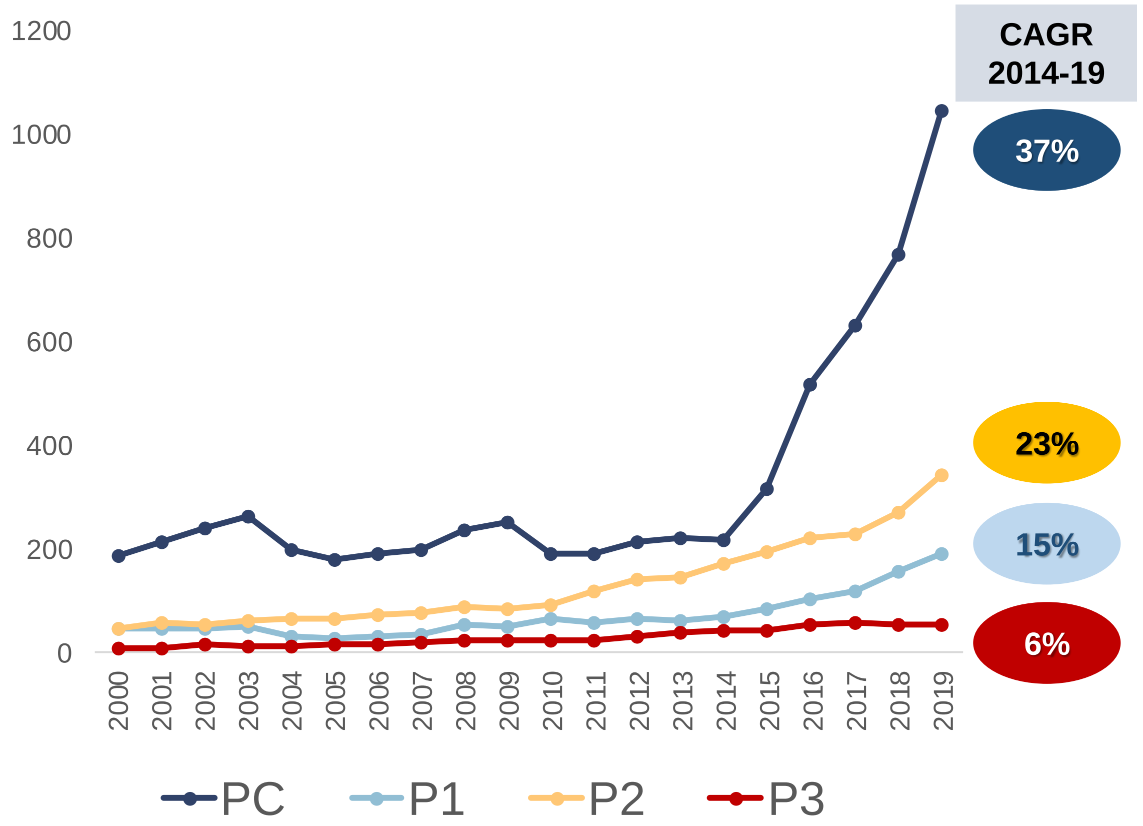
distributed bio

Next gen. platform delivering on a range of novel antibody modalities

Emerging demand for next-generation platforms for antibody and CAR-T therapeutics

C&GT: Significant Growth Opportunity

C&GT Pipeline by Phase



Biopharma industry investing heavily in this class of research due to its **broad clinical application** to treat a wide range of **diseases with unmet needs**

6 total — Therapies approved by FDA today; address key delivery, safety, and efficacy challenges

10-20 per year — **C&GTs** expected to be approved per year by 2025

>600 — **Active programs** for C&GT in clinical trials worldwide

~75% — Programs in **Phase I or earlier**, setting the stage for massive growth

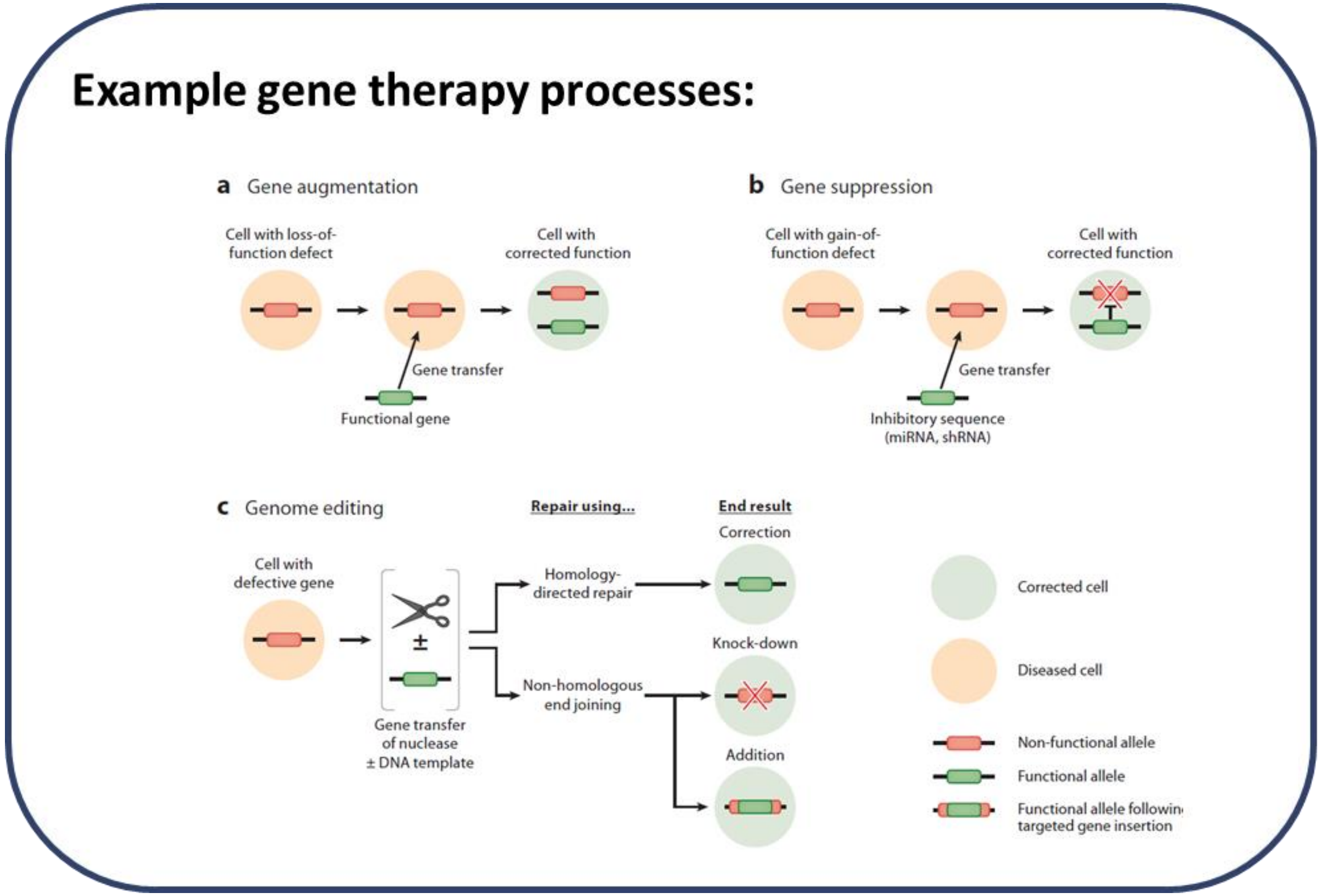
>200 per year — **IND** filings for C&GT expected to be received by 2020

$10.6B — Funding for **C&GT companies** in 2018 alone

Source: FDA, PricewaterhouseCoopers, PharmaProjects, Citeline, SVB.
FDA: https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics

C&GT Technologies

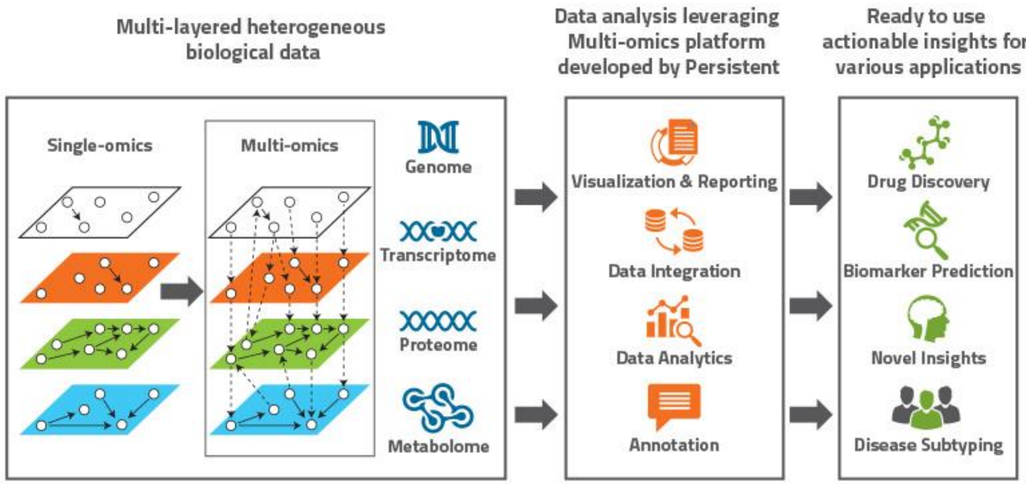
- CRL is a leader in C&GT safety assessment
  - Also have C&GT capabilities in Research Models, Discovery, Biologics, and Microbial Solutions
  - **~$100M** of current CRL C&GT annual revenue
- Areas for internal development and partnership include:
  - Hybrid efficacy and safety studies, next-gen. genotoxicity, plasmid & viral vector scale up for research and safety

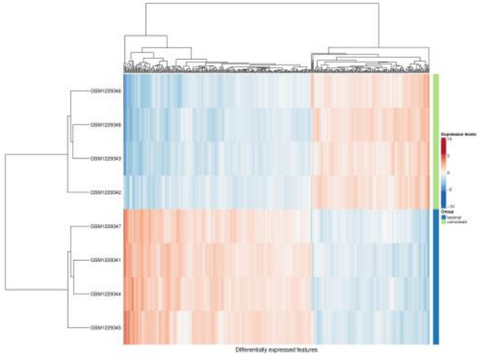


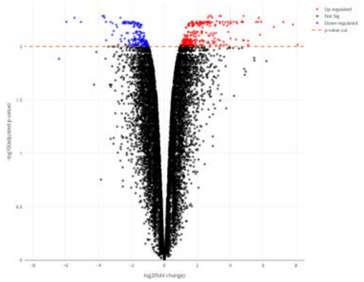
An opportunity to extend early-stage leadership in the C&GT market

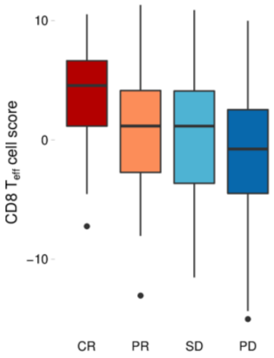
SCIENCE TREND #2:
The availability of human data has increased

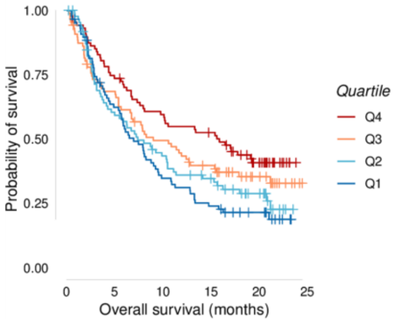
Deep phenotyping being undertaken at a single-cell level, in parallel, at scale:









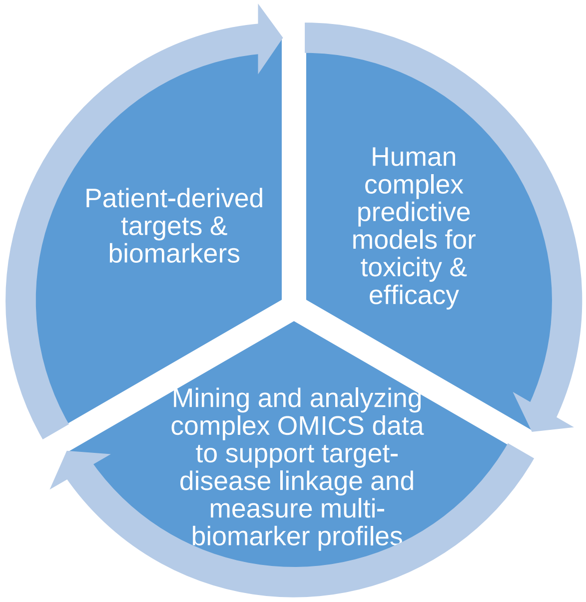


Human clinical and research data generation has boomed and enhanced our ability to mine, analyze, and interpret how our clients think about and use data

Human Translatability is Key Across All TAs

	Target discovery	Target validation	Lead generation & refinement	Pre-clinical development	
Goal	**Find target**	**Eliminate wrong target**	**Generate molecules**	**Eliminate molecule (toxicity)**	**Advance molecule (efficacy)**
Genetically engineered models	▪ Knockout ▪ Conditional knockout ▪ Knock-in (point mutation) ▪ Transgenic	▪ Knockout ▪ Conditional knockout ▪ Knock-in (point mutation) ▪ Transgenic	▪ Knock-in (reporter)	▪ Knockout ▪ Conditional knockout ▪ Humanized model	▪ Knockout ▪ Knock-in ▪ Transgenic ▪ Humanized model
Human Cells	▪ Human tissues ▪ Clinical data	▪ CRISPR ▪ RNAi ▪ iSPC-derived human cells ▪ Human tissues	▪ Disease-relevant cells for screening	▪ 3D, multicellular human models	▪ Human *in vitro* organ tox

Human biomarkers



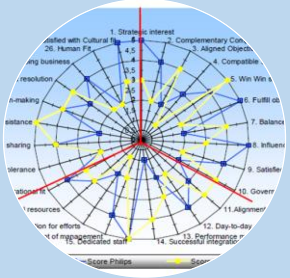
Decisions around target, biomarkers, and patient populations will be driven by complex combination of human data

Therapeutic Pillars

	Oncology	Immunology	Neuroscience
Discovery Market	$500M, 14% CAGR	$300M, 18% CAGR	$200M, 4% CAGR
Trends	▪ Human data, human cell models humanized *in vivo* models ▪ Combinations discovery & diagnostics ▪ CAR-T	▪ Immuno-oncology ▪ Neuroinflammation ▪ Microbiome ▪ Immunotoxicity	▪ Biologic therapeutics in CNS ▪ Modelling human disease *in vitro* ▪ New strategies for dementia ▪ R&O strategies
CRL response	▪ Bioinformatics ▪ 3D human models ▪ Gene expression technologies	▪ Sophisticated *in vitro* human assays covering target engagement & biomarkers ▪ Gene expression technologies ▪ Predictive immunotoxicity assays	▪ Delivery of biologics thru BBB ▪ iPSC-derived human CNS cells ▪ 3D human cellular models ▪ Gene expression technologies

CRL has additional runway for growth among main TAs and can further differentiate with focus on human assays

Partnerships are Key to Our Technology Strategy

Scouting	Deals	Execution	Health Checks
			
▪ VC fund partners ▪ Clients ▪ Automated tools	▪ Exclusive in CRO field ▪ 3- to 5-year term ▪ Sales & Marketing leverage from CRL ▪ Joint innovation ▪ Accretive during partnership	▪ Accountable lead ▪ Functional leads ▪ JSC governance	▪ Scorecards ▪ KPIs ▪ Client feedback

Building a technology partnership competence to support insight-driven M&A