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Integrated Product and Process Design

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PDA Southern California
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OVERVIEW

Biologics

Product and Process Design

Scientific Knowledge Integration

What is Coming Next

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Biologics (FDA)

Biologicals (EMEA)

Definition

- Vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins

- May be produced by biotechnology methods and other cutting-edge technologies

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Biologics

Trends

- **Pharmaceutical products** used to diagnose, cure, treat, or prevent disease state
- **Targeted/Tailored therapies** inhibits the metabolic pathway that underlies the disease
- **Personalized/Precision medicine for** diagnosis and specific treatment based individual's DNA

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Targeted oncology

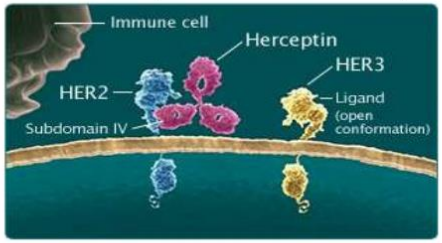
Immuno-oncology

Biologics

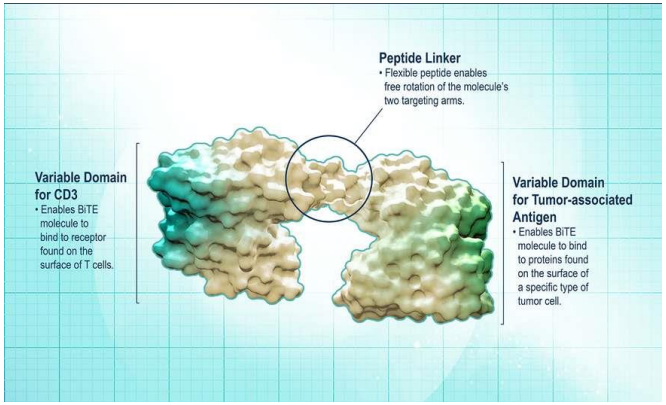
Modalities

Trastuzumab (Herceptin®) - MoA

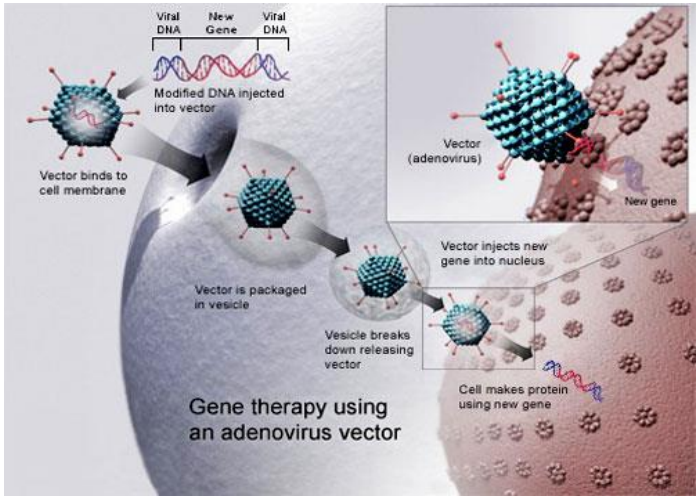
3. Trastuzumab (Herceptin®) binds to subdomain IV prevents dimerization; ADCC



http://www.perjeta.com/hcp/moa



Cell/Gene therapy



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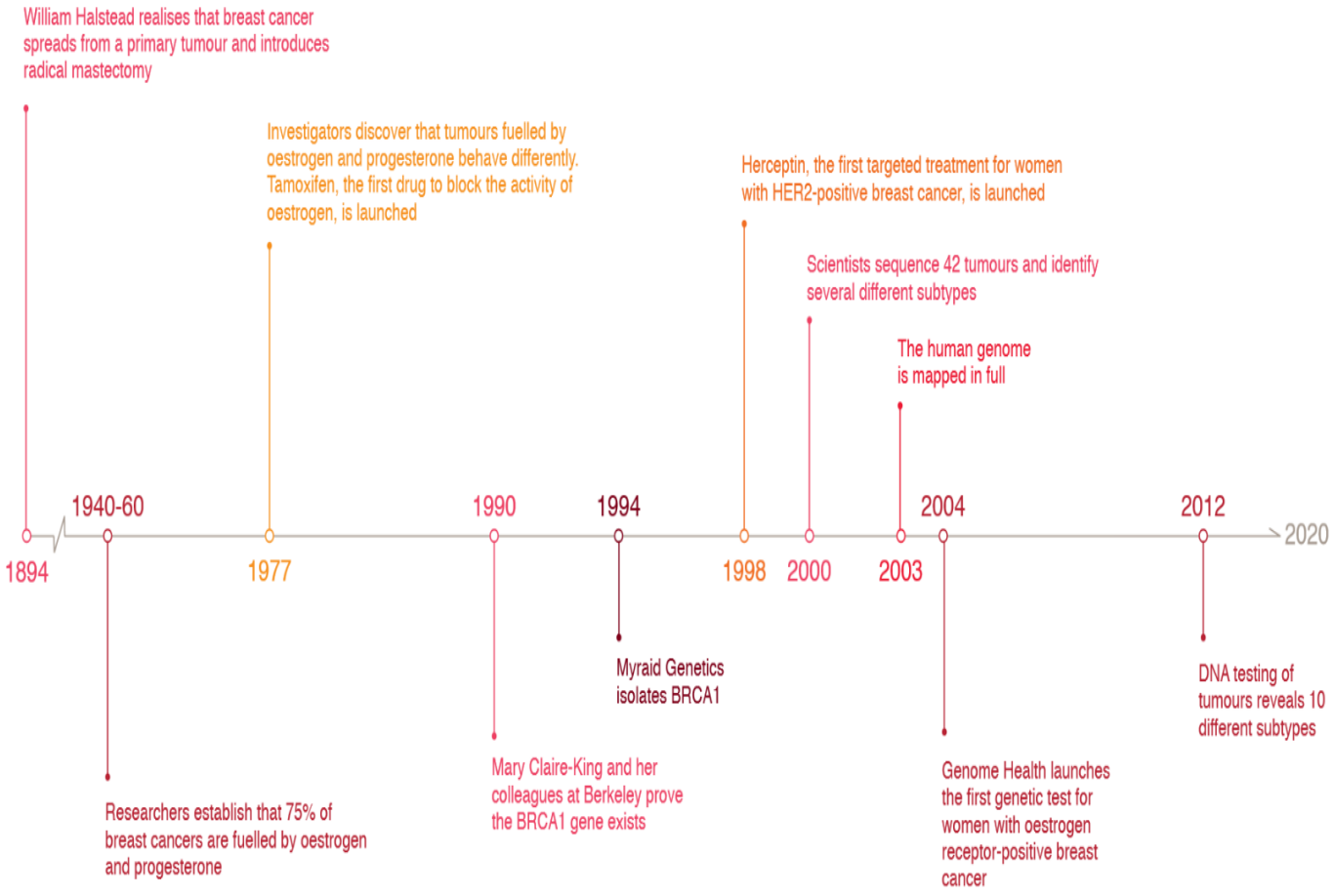
Biologics

Therapy



Source: PwC

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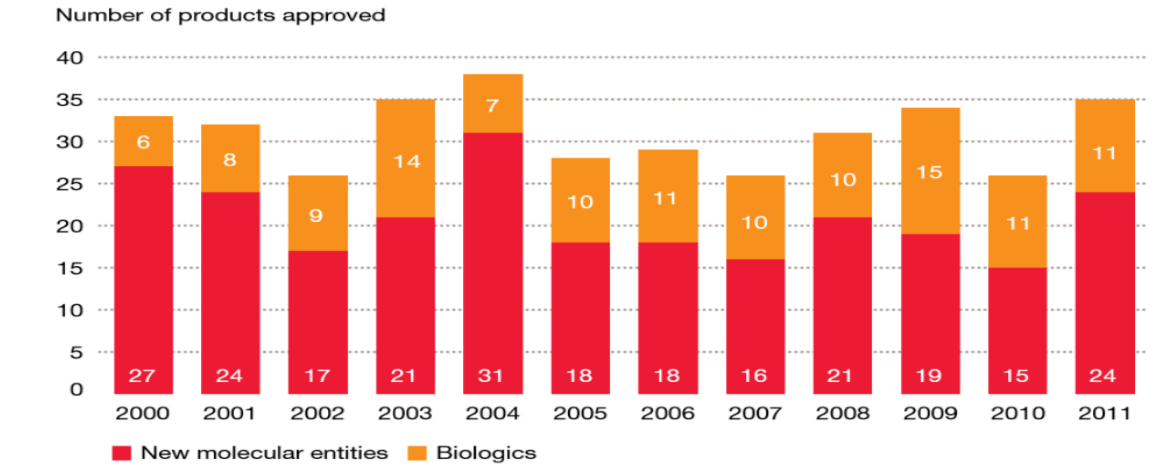
Biologics

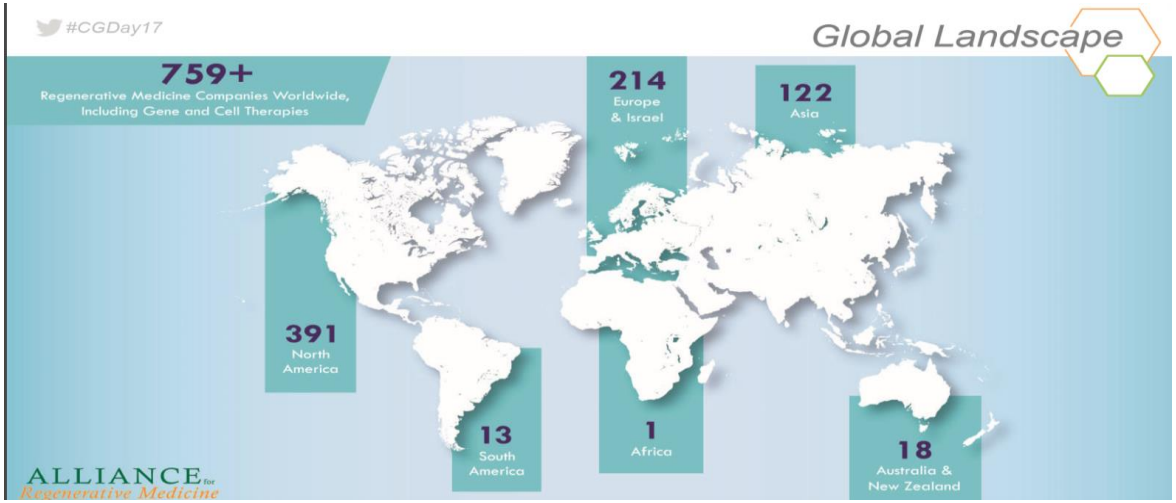
Therapy

Regenerative Medicine



Source: EvaluatePharma, 'World Preview 2018' (June 2012)

Regenerative Medicine: 760 companies and clinics of all sizes and 20 products approved by FDA



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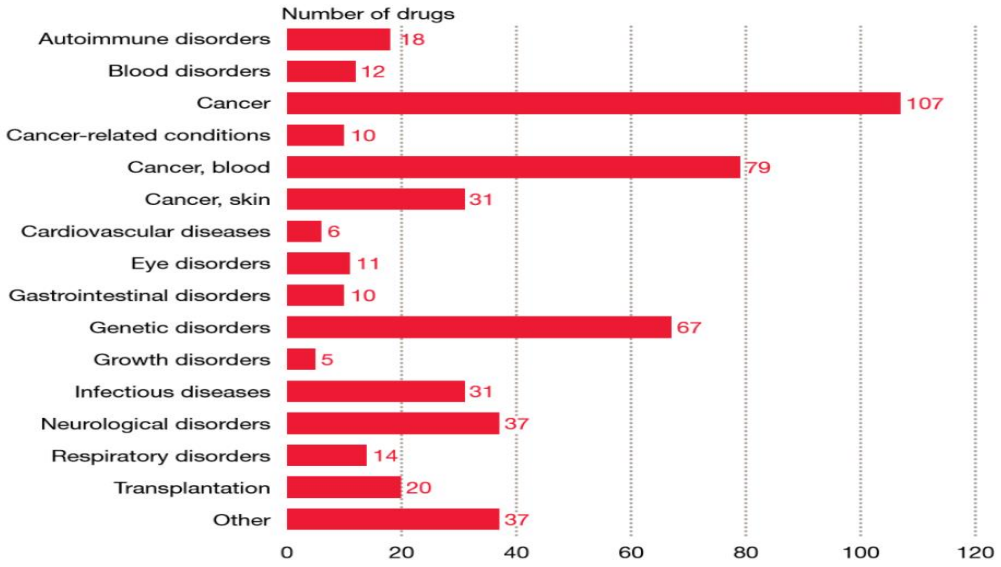
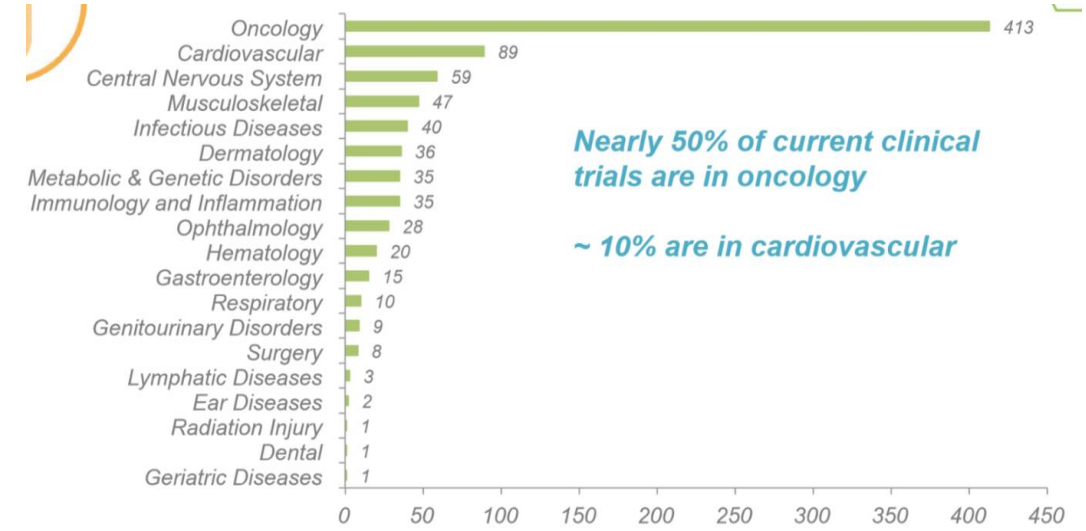
Biologics

Therapy



Source: PhRMA



Source: Alliance for Regenerative Medicine

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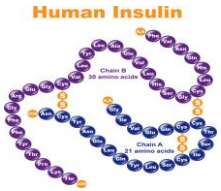
Biologics

Impact

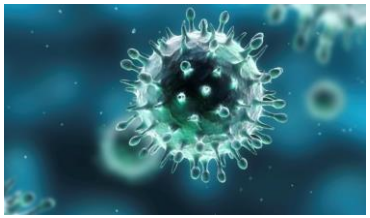
- Insulin



- aPC (Xigris)

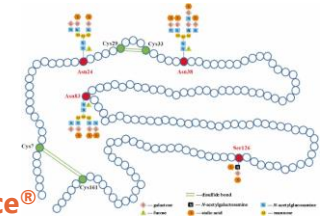
- Forteo

- Imlygic



IMLYGIC®
(talimogene laherparepvec)
INTRALESIONAL INJECTION

- Epogen



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OVERVIEW

Biologics

Product Design and Development

Scientific Knowledge Integration

What is Coming Next

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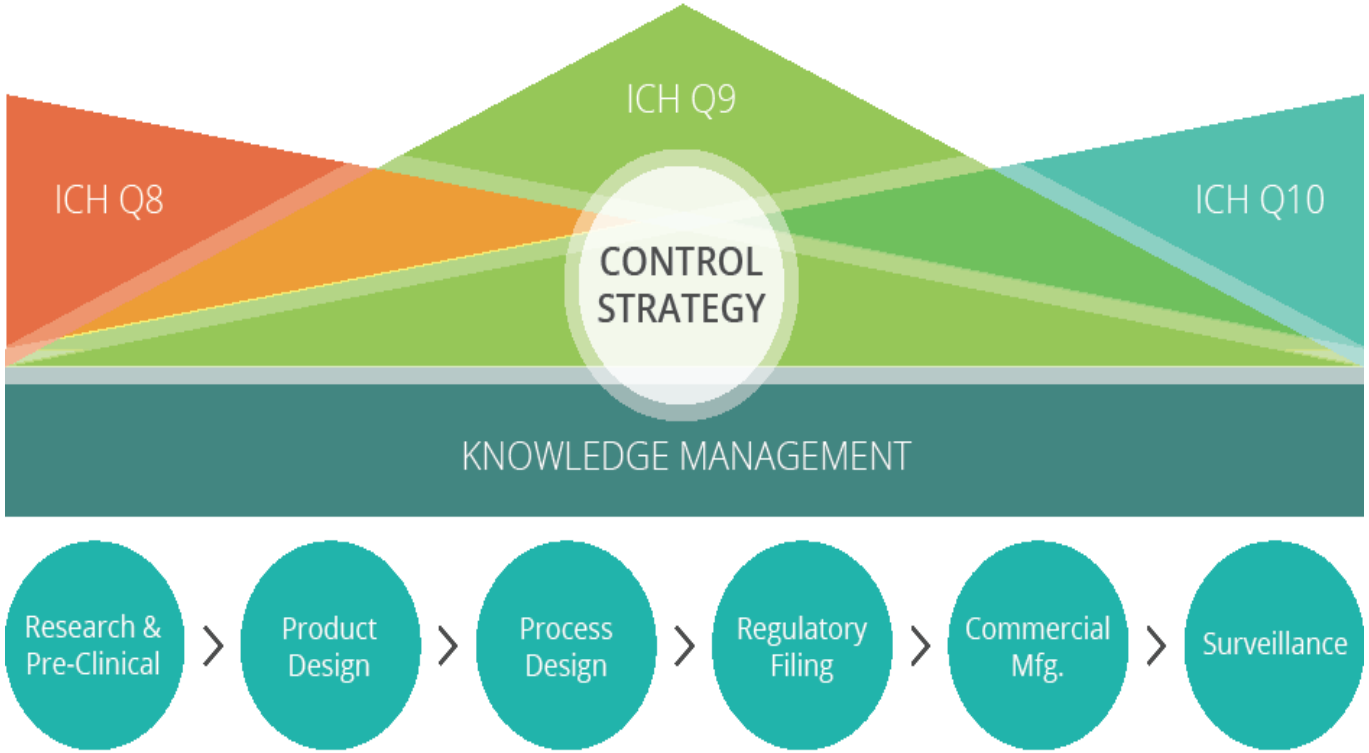
Product and Process Design

Model



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Product and Process Design

Patient Focus

- A patient centric development model with early considerations for a successful **Target Product Profile** will require using new paradigms

- Patient - Product Delivery
- Therapeutic Value - Outcomes
- Stronger Scientific Base for Development for Biologics

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Product and Process Design

Review

- # Target Product Profile

Asset Development: R&D-Tox-Ph I-Ph II-Ph III-Commercial-BLA/NDA

Purpose	Begin with the end in mind! Goals of the effective drug development, labeling claims (Sponsor/FDA)
Attributes	Statement of overall intent organized using key sections of the drug labeling (dymamic, changes and knowledge increase)
Advantages	Useful in pre-NDA, pre-BLA; tool for effective program management
	TPP summary does not represent a commitment or an obligation to consider the resultant evidence as adequate to achieve approval
	Proven to be effectively used in integrating all desired outcomes : Business, Clinical, Product/Process Development
Drives Molecule, Product and Process Characterization (Deep Dive)	

- Molecule/Modality (API)
- Dosage form/Delivery (DP, Drug Delivery)
- Therapy /Administration (Clinical)
- Stability and Use (Safety, Supply Chain)
- Market/ Product life cycle (Healthcare, Value..)

Commercial-Supply-Availability-Region- Patient: **Health Care Benefit**

2007: Draft FDA Guidance for Industry and Review Staff Target Product Profile — A Strategic Development Process Tool

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Product and Process Design

Review

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Product and Process Design

Review

Gate 1- Initiate Commercial Design	Gate 2-Confirm Design Options
• Marketing Requirements • Molecule Assessment • Target Product Profile • Standard product configuration • User Requirements (Combo products) • Injection Systems /Fit to network or CMOss	• Commercial Formulation stability • Clinical administration needs/patient data • Process Fit assessment • Analytical Methods fit assessment • Proposed Primary Container • Proposed Secondary packaging • Proposed shipper/distribution
• **Gate 0-FIH** • TPP SKU definition • In-use administration • FIH formulation , storage temperature • FIH fill strategy • Device technology	• **Gate 3-Design Optimization** • **Gate 4-Commercial Design** • **Gate 5-Design Validation** • **Gate 6-Design Performance** • **Gate 7-Design Change**

Asset Development: R&D-Tox-Ph I-Ph II-Ph III-Commercial-BLA/NDA

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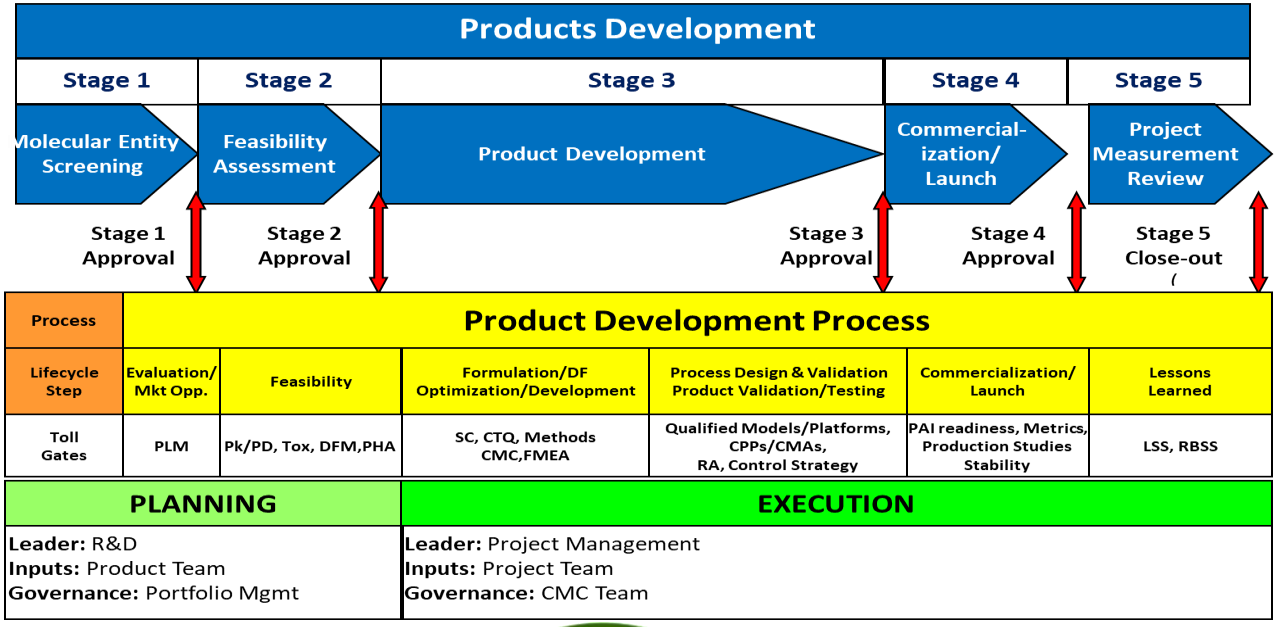
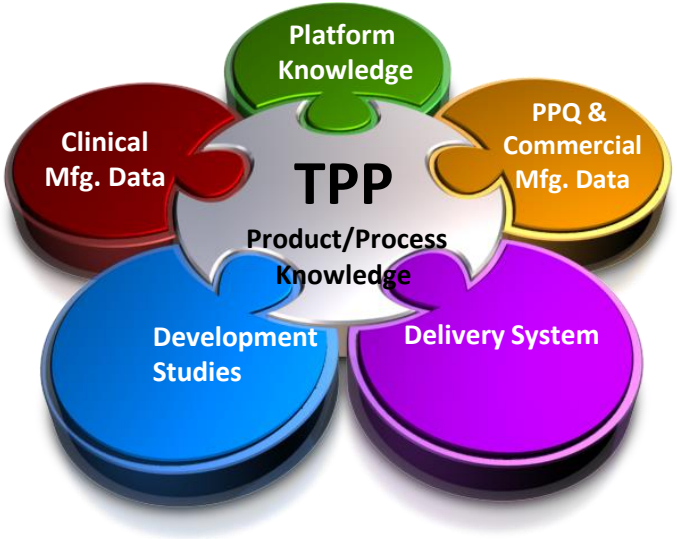
Product and Process Design

Review





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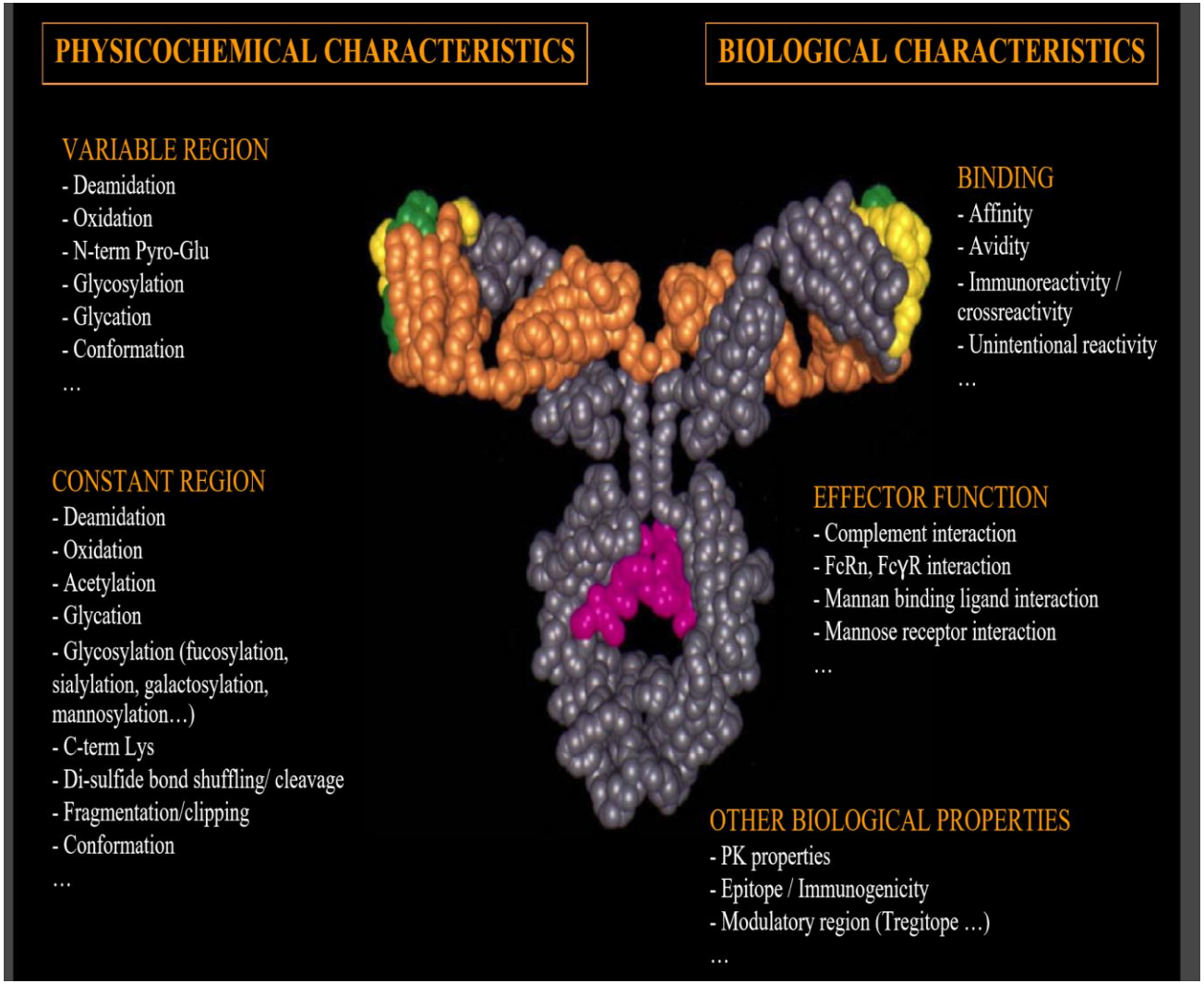
Product and Process Design

Product



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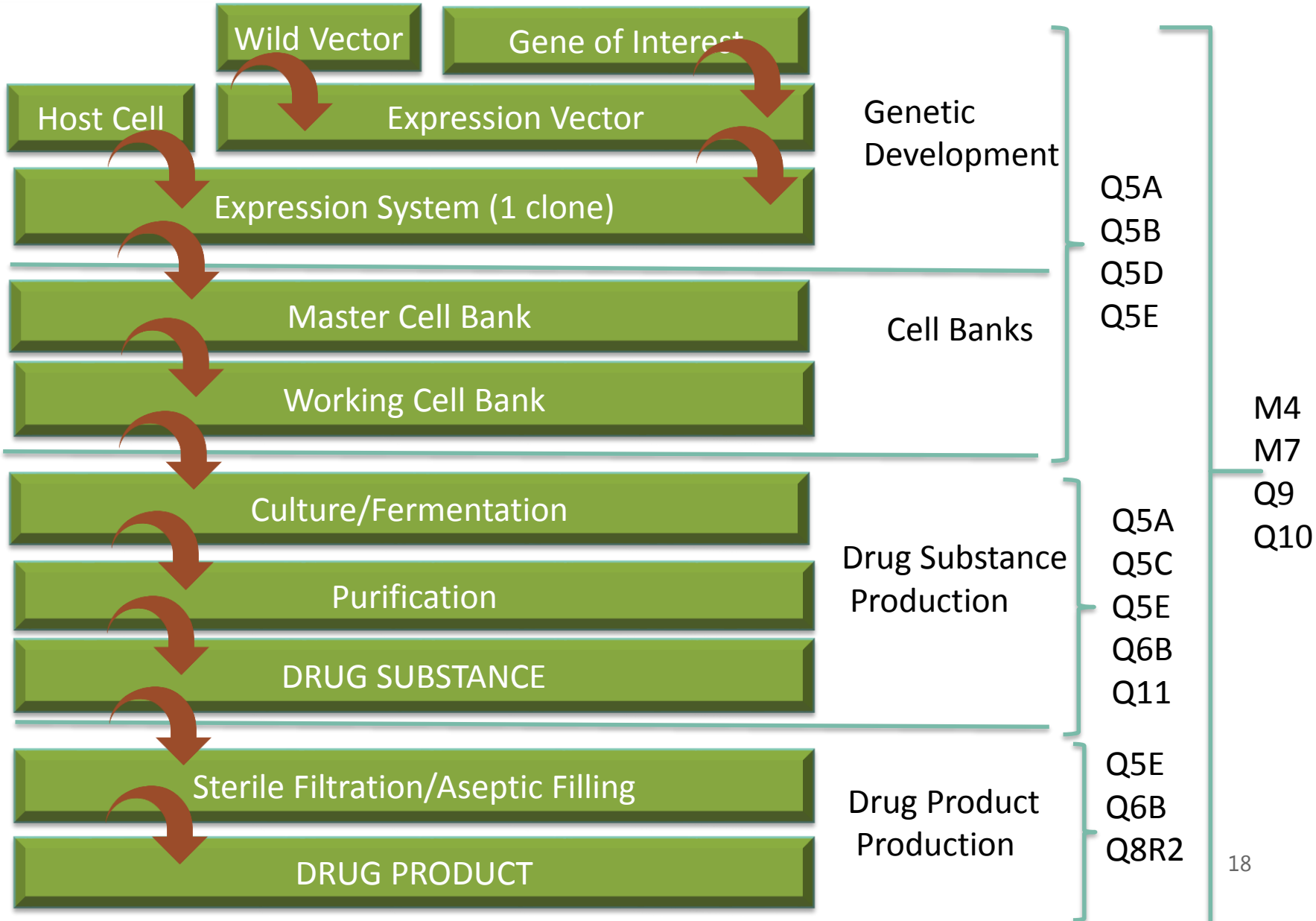

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Product and Process Design

Process

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Product and Process Design

Product Delivery

https://www.slideshare.net/team_medical/lowering-the-hurdles-in-device-selection-for-biologics

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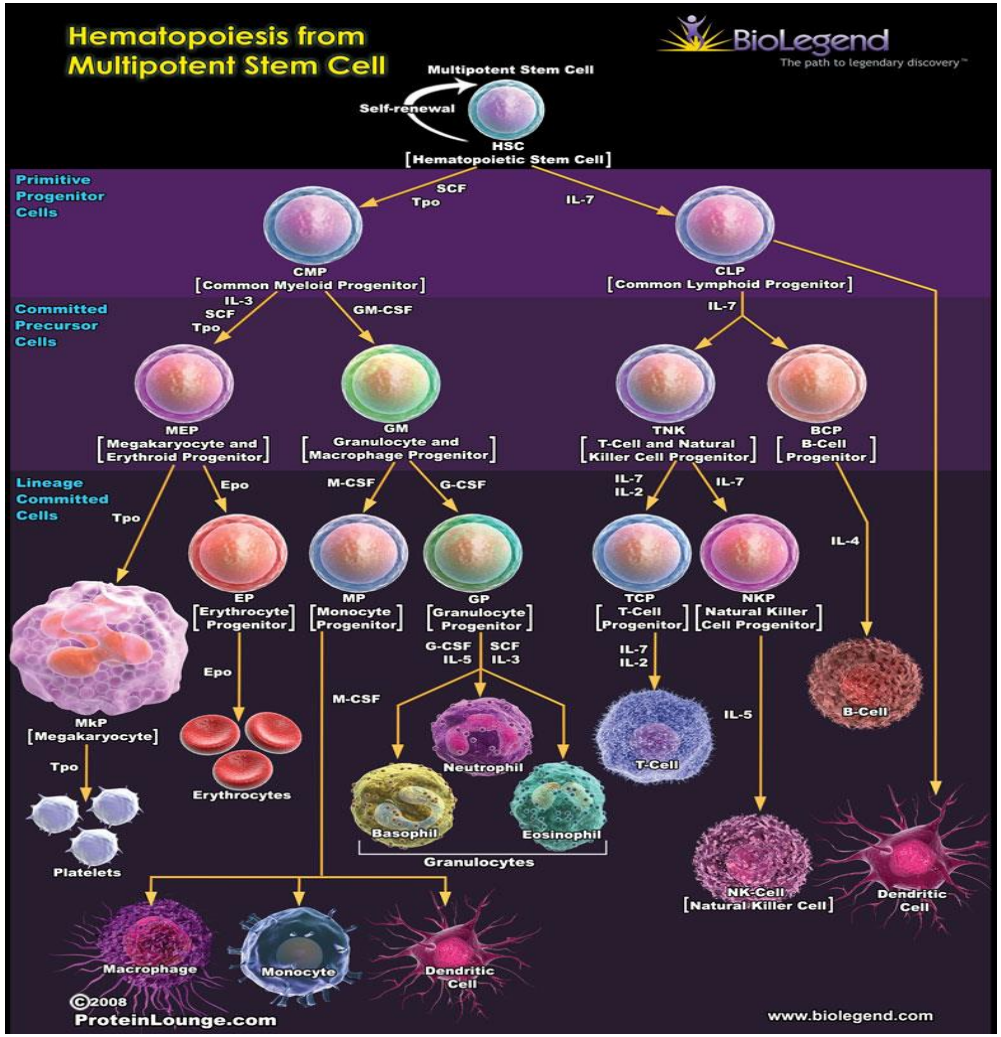
Product and Process Design

Product



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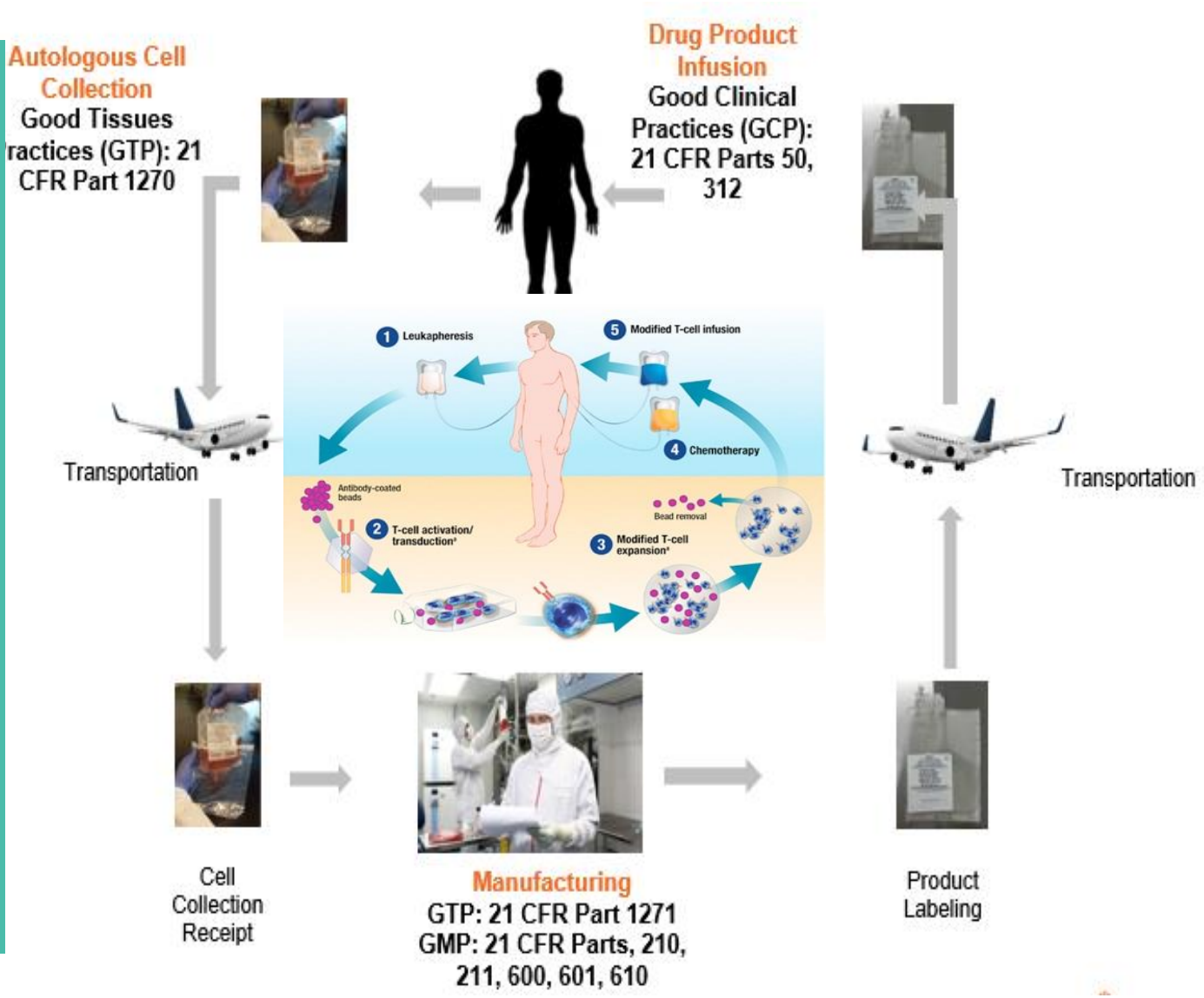
Product and Process Design

Process



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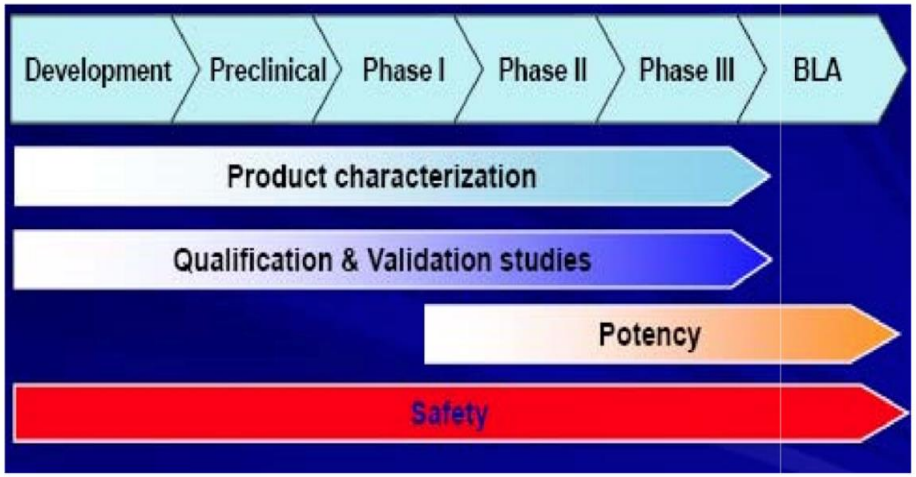
Product and Process Design

Quality Target Product Profile (QTPP)

- Therapy type: allogenic, autologous
- Genotype, Cell identity
- Final product viability
- Desired potency
- Quantity (cells)
- Purity/ Impurities to be eliminated
- Stability/Storage Conditions



QbD Starts In Discovery Phase for a Cell Therapy Product

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OVERVIEW

Biologics

Product Design and Development

Scientific Knowledge Integration

What is Coming Next

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Scientific Knowledge Integration

- Governance
  - Product /Franchise Level
  - CMC Level (Cross functional)
  - Quality Management Level
  - Decision Making Level
- Tools
  - Technical: CMC Documents at each “gate”
  - Big Data: Sources, Analytics, Modeling
  - Platforms: Leverage previous success
  - Risk Management tools

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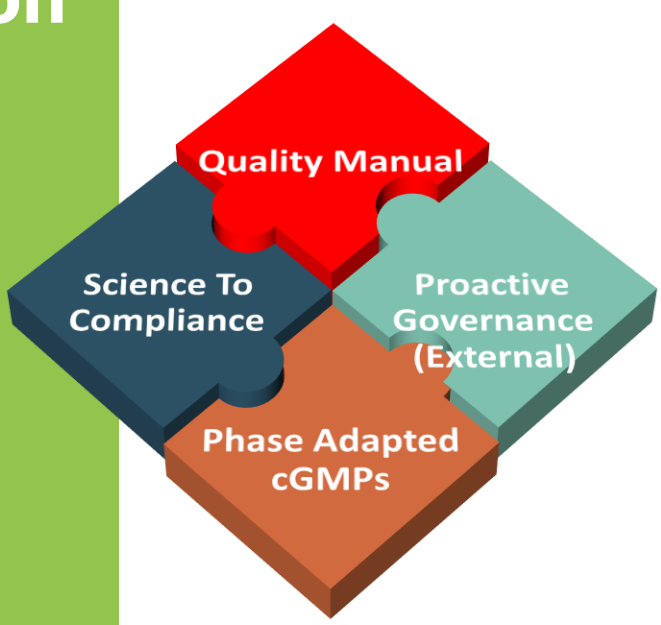
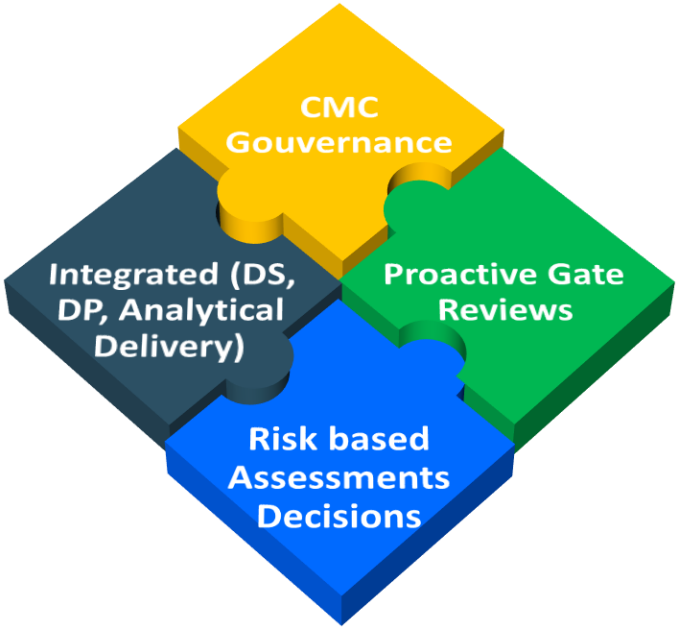
Scientific Knowledge Integration

- CMC Governance
- Quality Management Level





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Scientific Knowledge Integration

- Knowledge Generation
  - Internal & External

	R&D	Pre-Clinical	Phase 1	Phase 2	Phase 3	Commercial
Molecular biology Genomics, Chemistry,	Discovery laboratories, University Labs, Medical centers, Specialized Technology labs, CROs					
Tox studies ADME		Pre-clinical labs, in-vivo labs, animal tox facilities				
Analytical Dev DS, DP, Stability	R&D development labs,Regional sites, Regional CROs, CDMOs, QC labs,					
Molecule, Modality or Technology Dev	Labs, CROs, CDMOs, characterization , stability, stress testing, in-vitro development modeling					
Formulation Development	CRO, CDMOs specialized on one or multiple formulation platforms: Injectable (liquid, lyo, infusion, nanoparticles, long release) oral, transdermal, buccal, etc					
Delivery System Development	CDMOs and CMOs Injectable delivery systems, medical devices specialized on selected technologies (pumps, autoinjectors, electronic devices,					
API Process Development		CRO, CDMOs CMOs Facilities, Equipment, Engineering services, Statistics and Modeling				
Drug Product Process Development		CRO, CDMO, CMOs Facilities, Equipment, Engineering services, Unit operation characterization and Modeling				
Clinical Materials: manufacturing, packaging		CDMOs CMOs, QC laboratories (release, stability)				
Consulting Services	Clinical Development, Regulatory Affairs, Product and Process Development, Facilities Design, Due diligence, Business operations, Project management, Quality and Compliance, IT and Data management (data integrity, data security)…					

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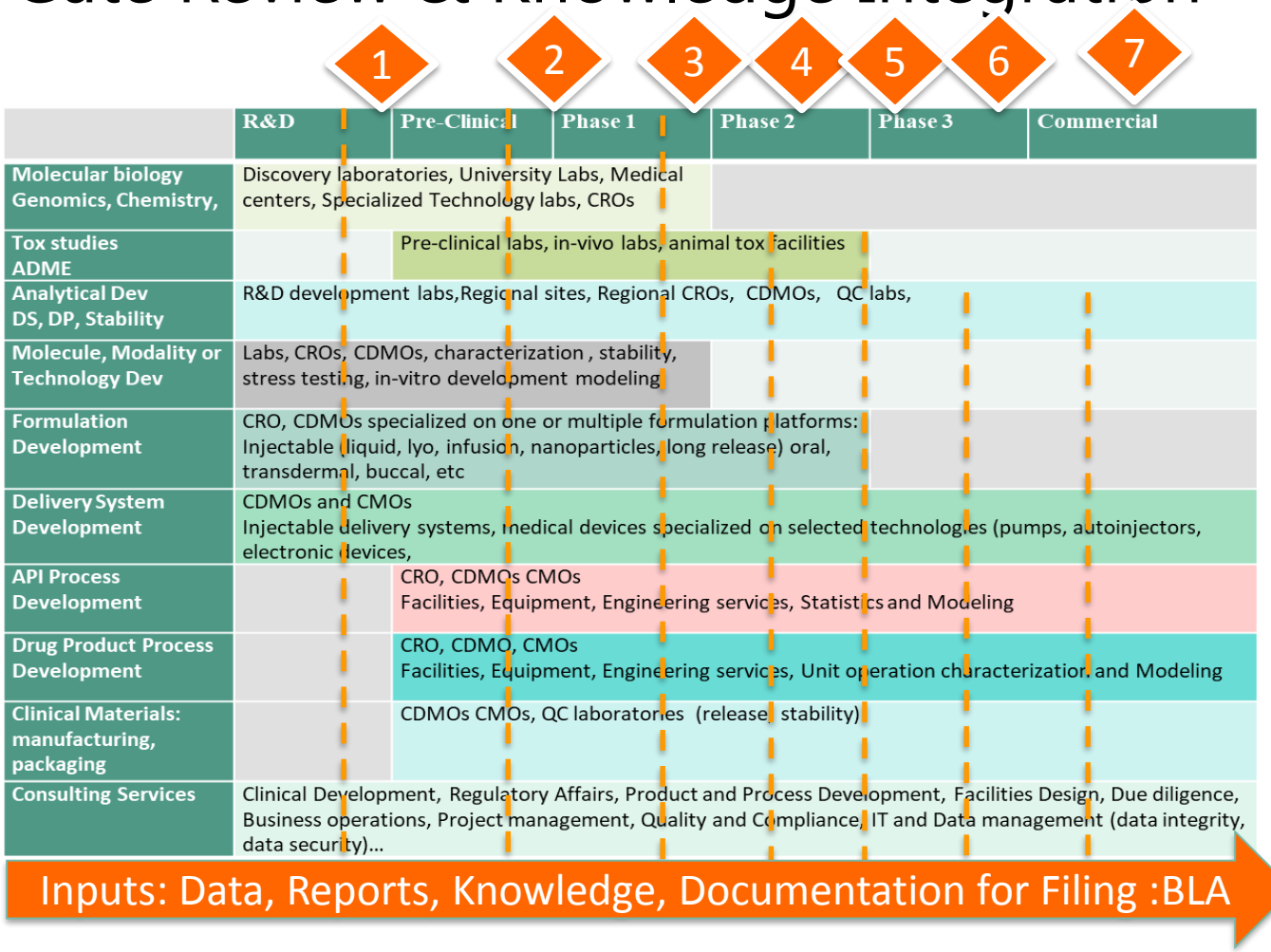
Scientific Knowledge Integration

Gate Review & Knowledge Integration



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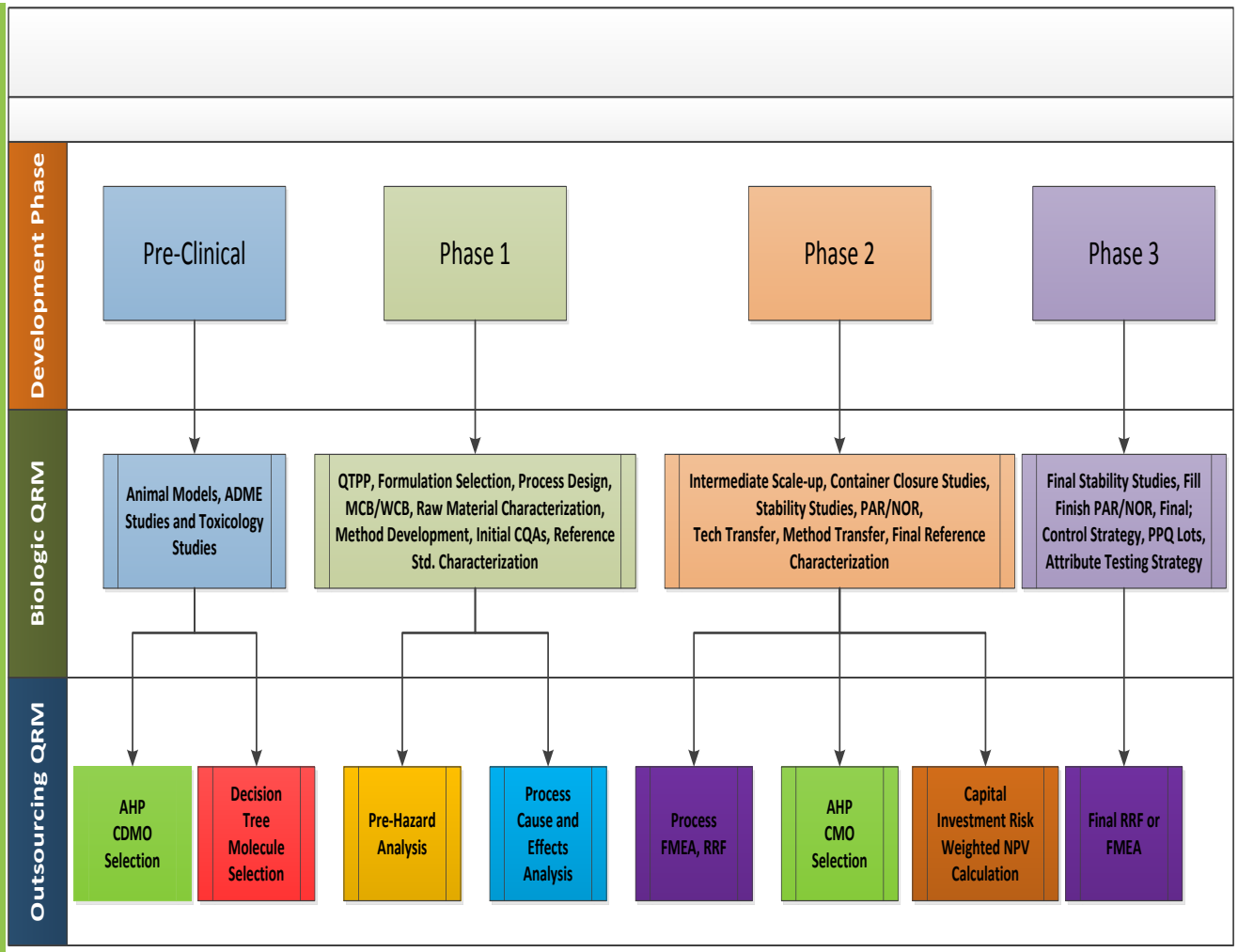
Scientific Knowledge Integration



Risk Assessment Tool- Program Management

Risks

A. Bioassay results
B. Sterile filtration
C. Oxidation lot x
D. Aggregation
E. Freeze–thaw modifications
F. pH change during shipment on dry

Impact Assessment

		IMPACT				
		Low	Minor	Moderate	Major	Severe
		1	3	5	7	9
Likelihood	Very likely 9				A	
	Likely 7		E	B		
	Possible 5		D	C		
	Unlikely 3					
	Remote 1					

Low	Take These Risks
Medium	Consider Having Mitigations or contingency plan
High	Have Mitigation/contingency plan

Mitigations

A. Alternate assay development at CRO
B. Filter re-validation
C. RCA-materials in direct contact
D. Design studies at different level of silicone (Syringe)
E. Container integrity studies at freezing temperatures

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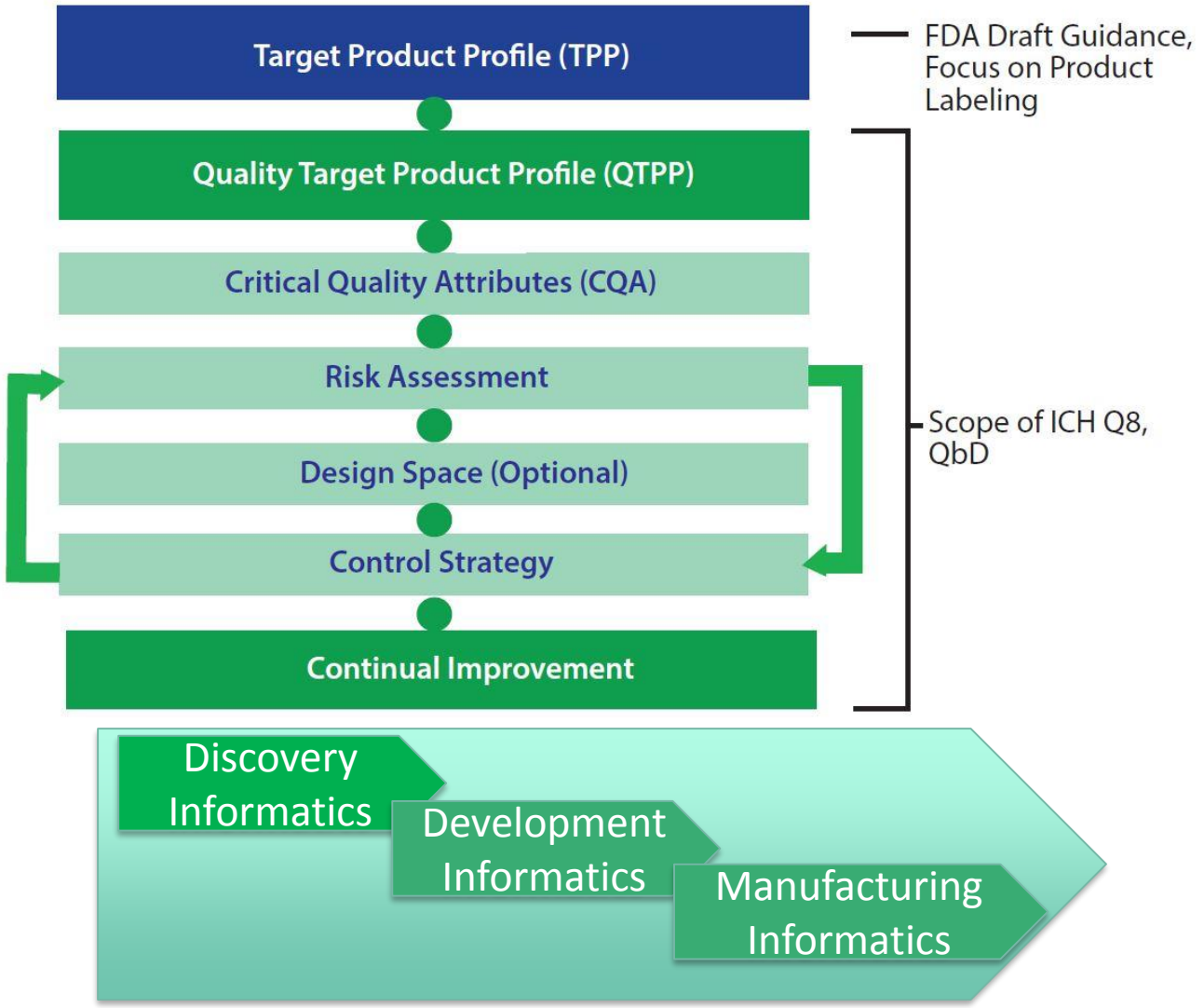
Scientific Knowledge Integration



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OVERVIEW

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Product Design and Development

Scientific Knowledge Integration

What is Coming Next

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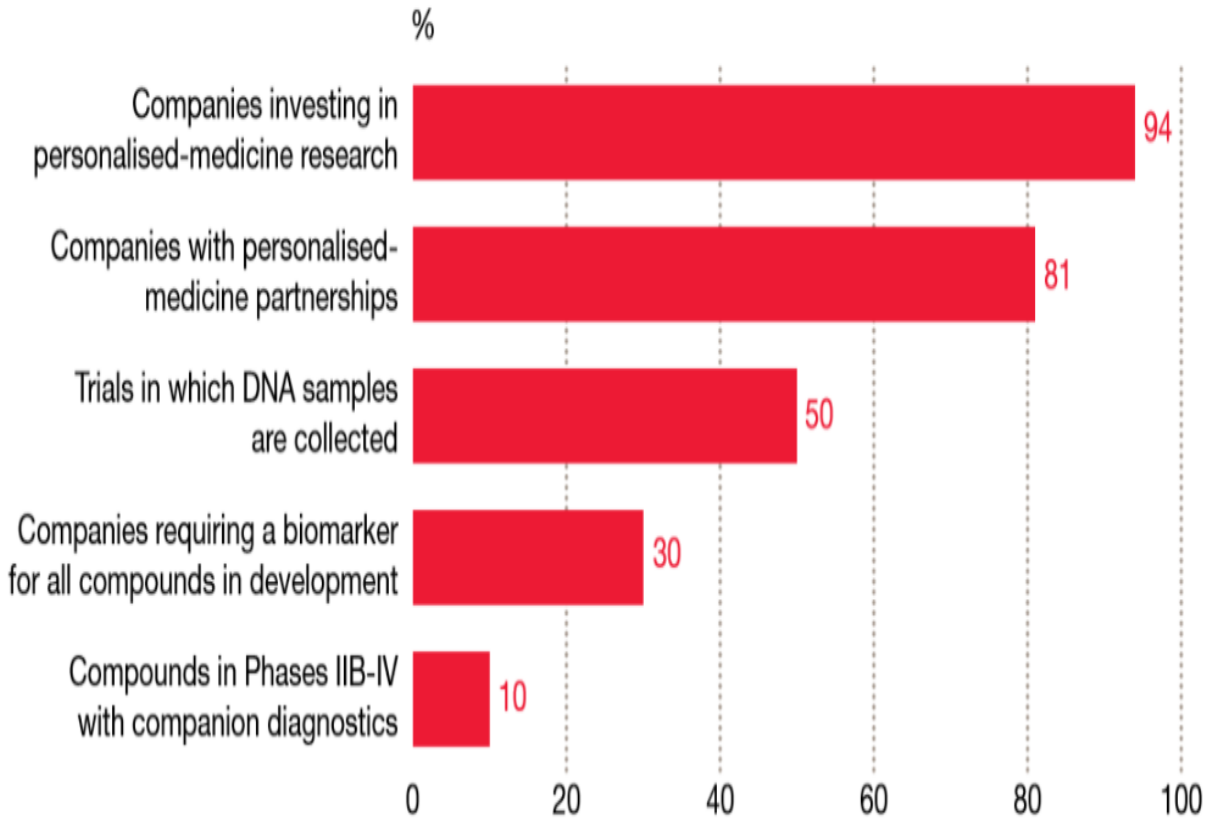
What is Coming Next



Source: Tufts Center for the Study of Drug Development

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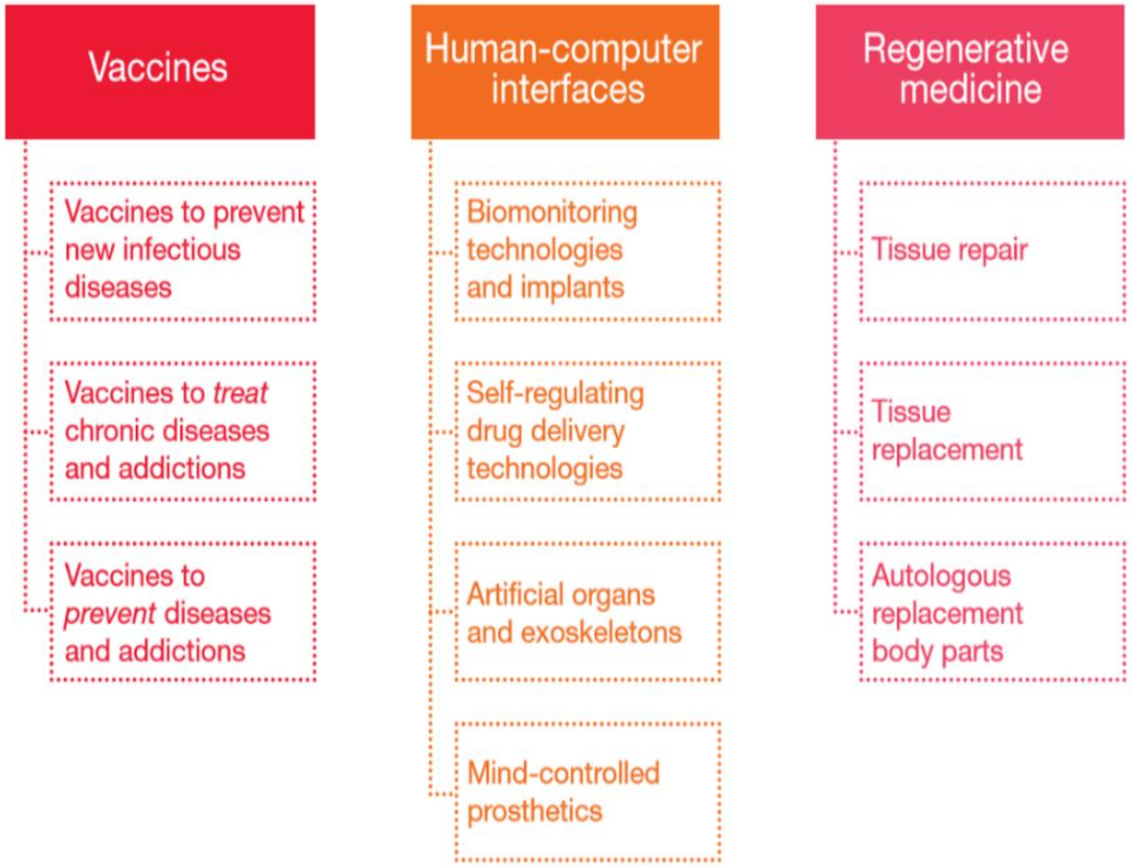
What is Coming Next



Source: PwC

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What is Coming Next

Every company will have to…

- **P**rovide real-world data on the outcomes
- **B**e selective about the diseases it addresses, new treatments
- **I**nvest more heavily in genetics and genomics
- **I**mprove its scientific productivity
- **G**et access to the best science and eliminate waste

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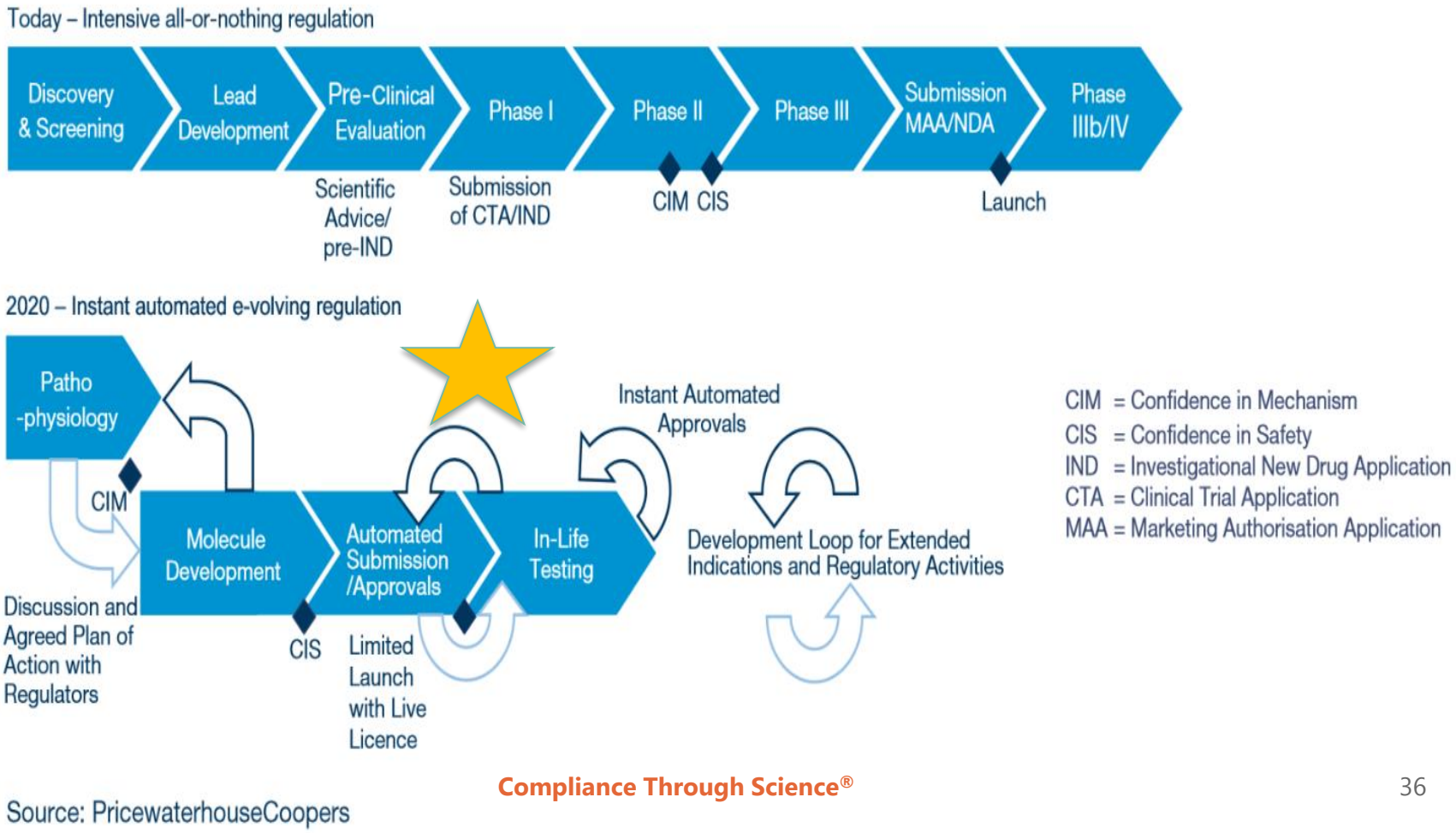
2020 Vision for Pharma



Source: PricewaterhouseCoopers

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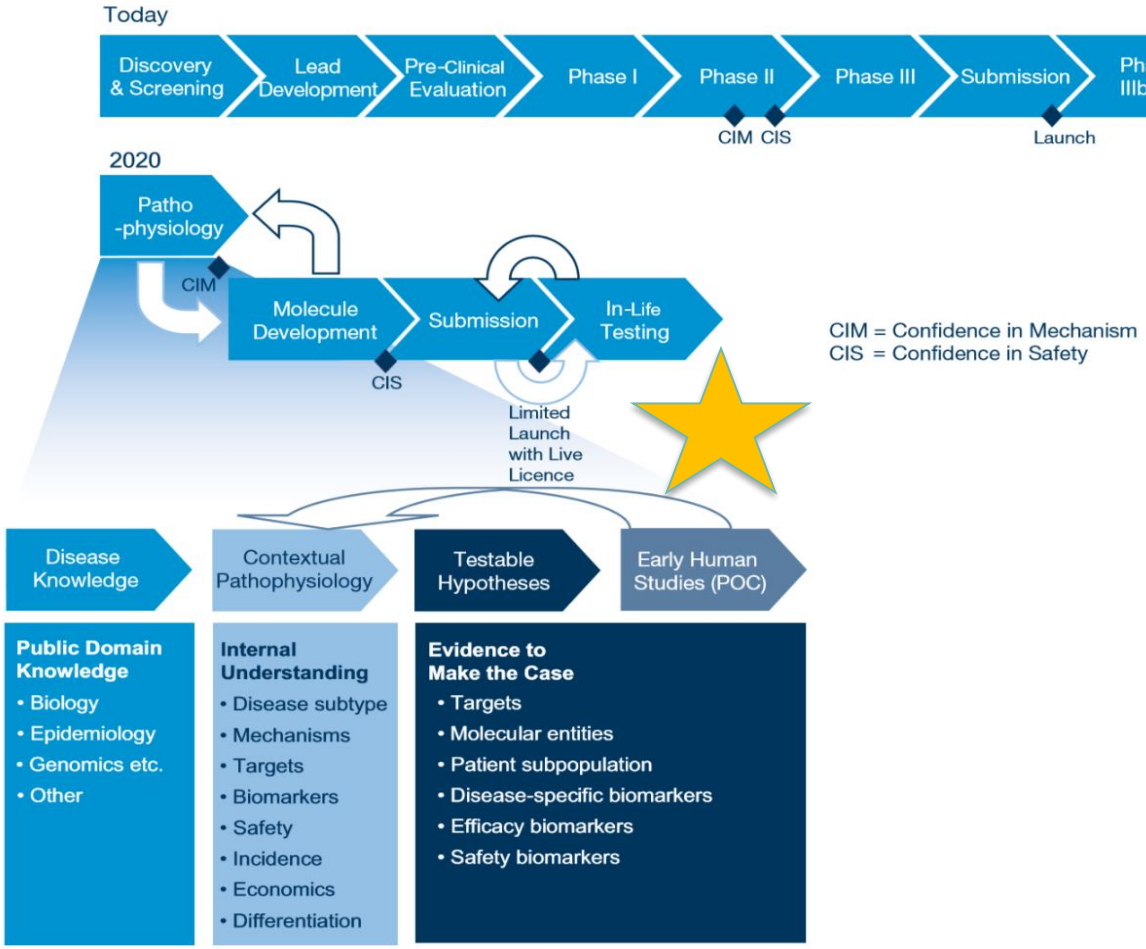
Modalities with Mechanism that Work



Source: PricewaterhouseCoopers

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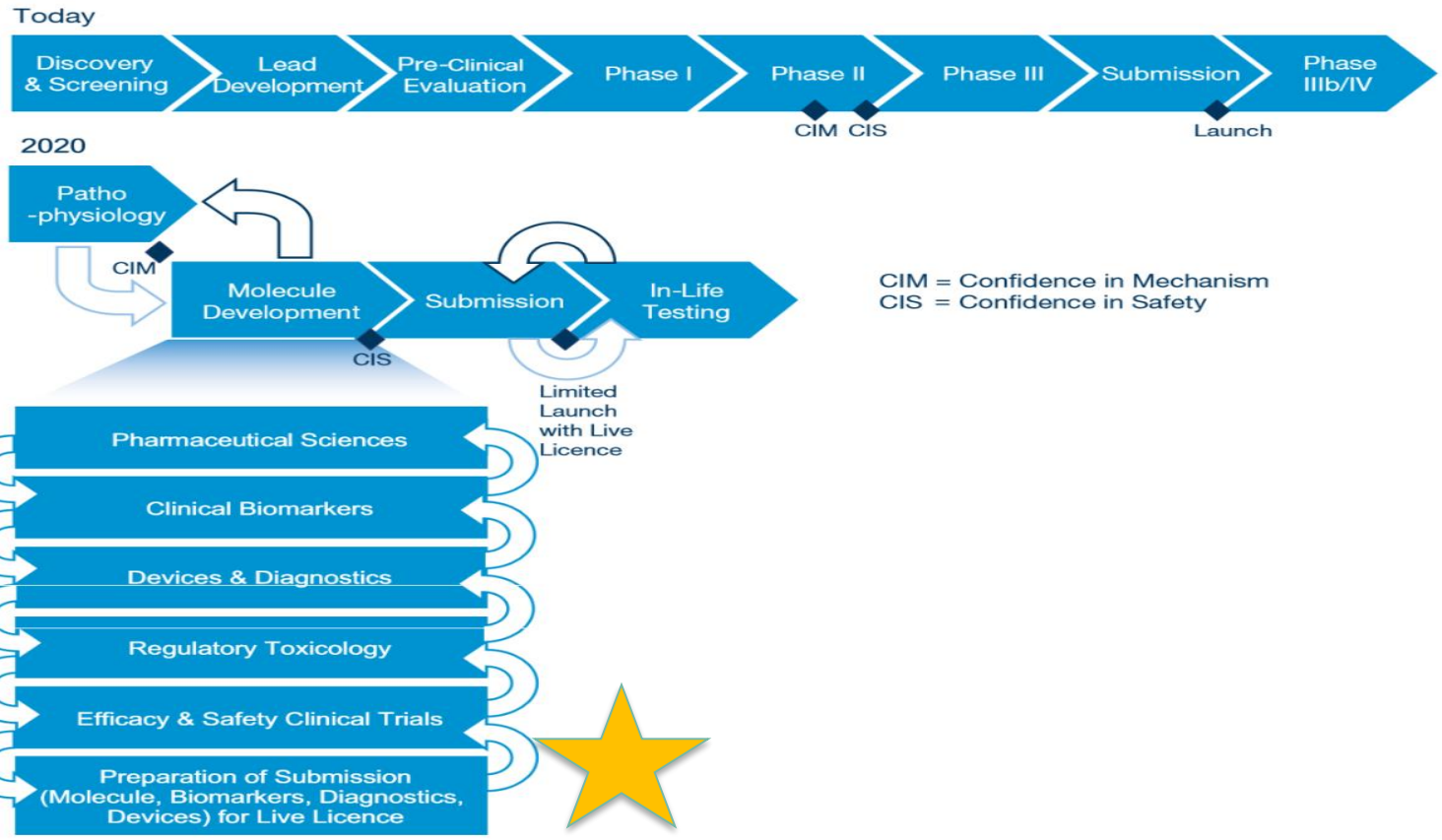
Any Time Anywhere Healthcare



Source: PricewaterhouseCoopers

Integrated Clinical Trials and Clinical Practice

TED Talks

We can reprogram life. How to do it wisely | Juan Enriquez
https://www.youtube.com/watch?v=bEdvQjTGYP8

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