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From Small Molecules to Sequences: Expanding the Informatics Landscape
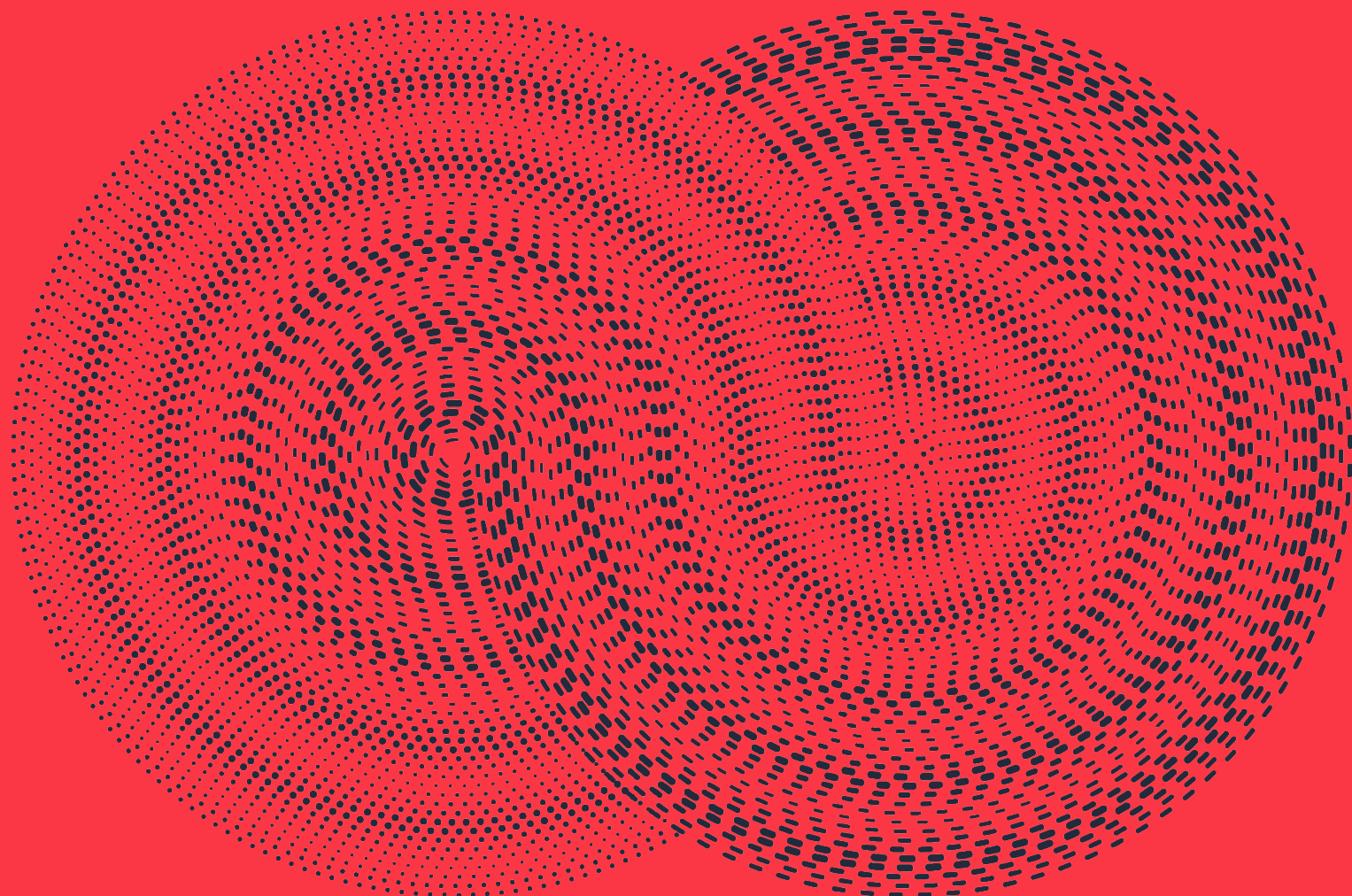
Adrian Stevens

Chemaxon

Chief Product Officer

From Small Molecules to Sequences:
Expanding the Informatics Landscape

Adrian Stevens
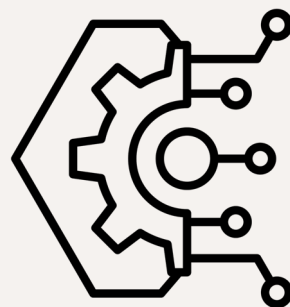Chief Product Officer, Chemaxon
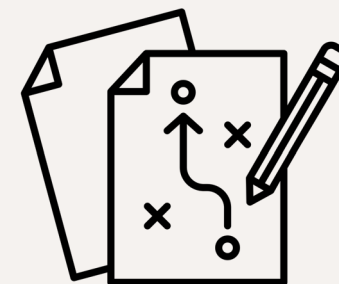
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Agenda

Growth of Biologics
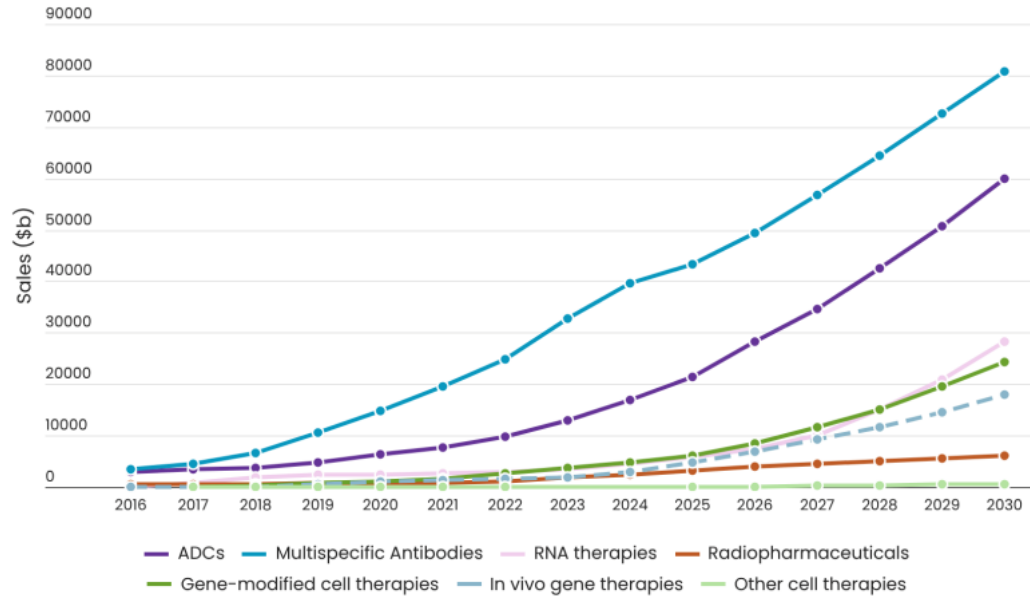
Chemaxon's Plan

First Steps

Growth of Biologics

Top 20 Drug Sales 2024

Rank	Drug Name	Disease Area	Modality	Manufacturer(s)	2024 Sales (Million USD)	Growth Rate 2023-2024 (%)
1	Keytruda (pembrolizumab)	Oncology	Antibody	Merck	29,482.0	17.9
2	Ozempic/Wegovy (semaglutide)	Metabolic Diseases	Synthetic Peptide	Novo Nordisk	25,892.9	40.6
3	Eliquis (apixaban)	Cardiovascular/Hematology	Small Molecule	Bristol Myers Squibb / Pfizer	20,703.0	9.2
4	Dupixent (dupilumab)	Immunology/Respiratory	Antibody	Sanofi/Regeneron	14,147.0	22.1
5	Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide)	Infectious Diseases (HIV)	Small Molecule	Gilead Sciences, Inc.	13,423.0	13.3
6	JARDIANCE family	Metabolic/Cardiovascular	Small Molecule	Boehringer Ingelheim / Eli Lilly	12,385.0	15.0
7	Skyrizi (risankizumab-rzaa)	Immunology	Antibody	AbbVie	11,718.0	50.9
8	Darzalex (daratumumab) & Darzalex Faspro (daratumumab and hyaluronidase-fihj)	Oncology/Hematology	Antibody	Johnson & Johnson	11,670.0	19.8
9	Mounjaro (tirzepatide)	Metabolic Diseases	Synthetic Peptide	Eli Lilly and Company	11,540.1	123.5
10	Stelara (ustekinumab)	Immunology	Antibody	Johnson & Johnson	10,361.0	-4.6
11	Trikafta/Kaftrio (elexacaftor/tezacaftor/ivacaftor)	Respiratory/Rare Disease	Small Molecules (3)	Vertex Pharmaceuticals Incorporated	10,238.6	14.5
12	Eylea (aflibercept)	Ophthalmology	Recombinant Fusion protein	Regeneron/Bayer	9,546.0	-25.9
13	Opdivo (nivolumab)	Oncology	Antibody	Bristol-Myers Squibb	9,304.0	3.3
14	Humira (adalimumab)	Immunology	Antibody	AbbVie	8,993.0	-37.6
15	Gardasil/Gardasil 9	Vaccines/Infectious Diseases	Recombinant vaccine	Merck	8,583.0	-3.4
16	Entresto (sacubitril/valsartan)	Cardiovascular	Small Molecules (2)	Novartis	7,822.0	29.6
17	Comirnaty (tozinameran)	Vaccines/Infectious Diseases	mRNA vaccine	Pfizer/BioNTech	7,785.1	-49.1
18	Farxiga/Forxiga (dapagliflozin)	Metabolic/Cardiovascular/Renal	Small Molecule	AstraZeneca	7,656.0	27.7
19	Ocrevus (ocrelizumab)	Neurology/Immunology	Antibody	Roche	7,654.9	7.8
20	Tagrisso (Osimertinib)	Oncology	Antibody	AzstraZeneca	6,580.0	13.5

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Growth of Biologics

Chart 12: Worldwide Sales by Modality

Sales ($b)

ADCs — Multispecific Antibodies — RNA therapies — Radiopharmaceuticals — Gene-modified cell therapies — In vivo gene therapies — Other cell therapies

Source: EvaluatePharma© (May 2025)

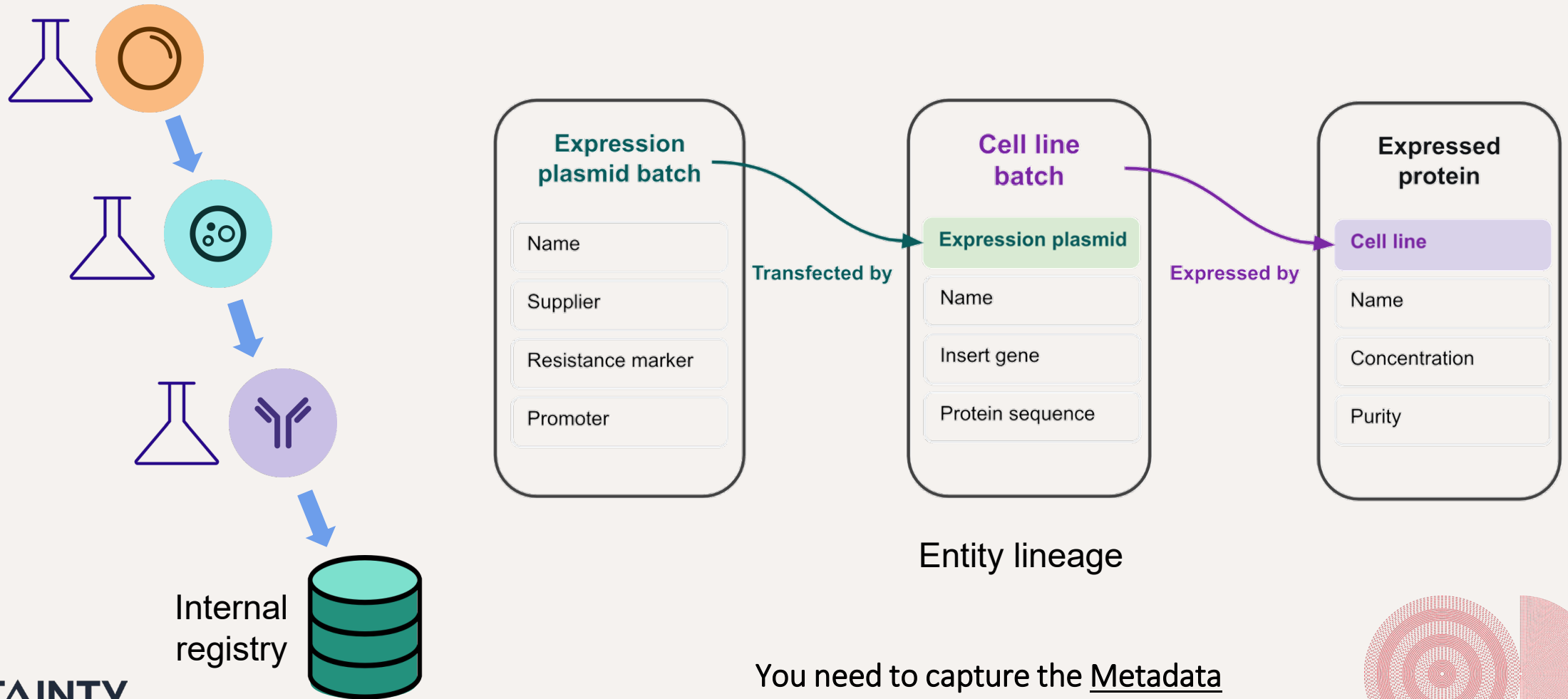- Value: Biologics have now overtaken small molecule drugs
  - 2025: 51% of all prescription drug sales
  - Expected to grow to 57% by 2030

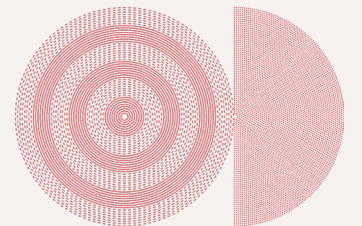Chart 14: Worldwide Prescription Drug Sales: Biotech vs. Conventional Technology

Biotechnology — Conventional
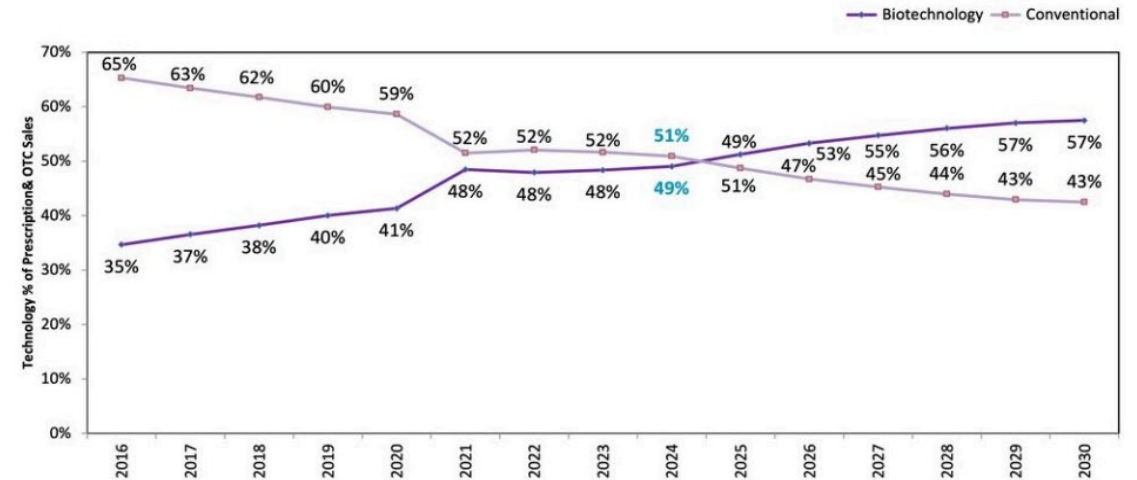
Source: Evaluate Pharma: World Preview (May 2025)

- Modalities: ADCs, bispecifics and peptides growing
  - GLP-1 inhibitors seeing fastest growth

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6

How a Biologic is Made = Just as Important as What!

Internal registry

Expression plasmid batch

- Name
- Supplier
- Resistance marker
- Promoter

Transfected by

Cell line batch

- Expression plasmid
- Name
- Insert gene
- Protein sequence

Expressed by

Expressed protein

- Cell line
- Name
- Concentration
- Purity

Entity lineage

You need to capture the Metadata associated with the creation of the entity

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Biological Therapeutics are becoming more Sophisticated

IgG Antibody

ScFvs

Fabs

ADCs

Bispecifics

?!
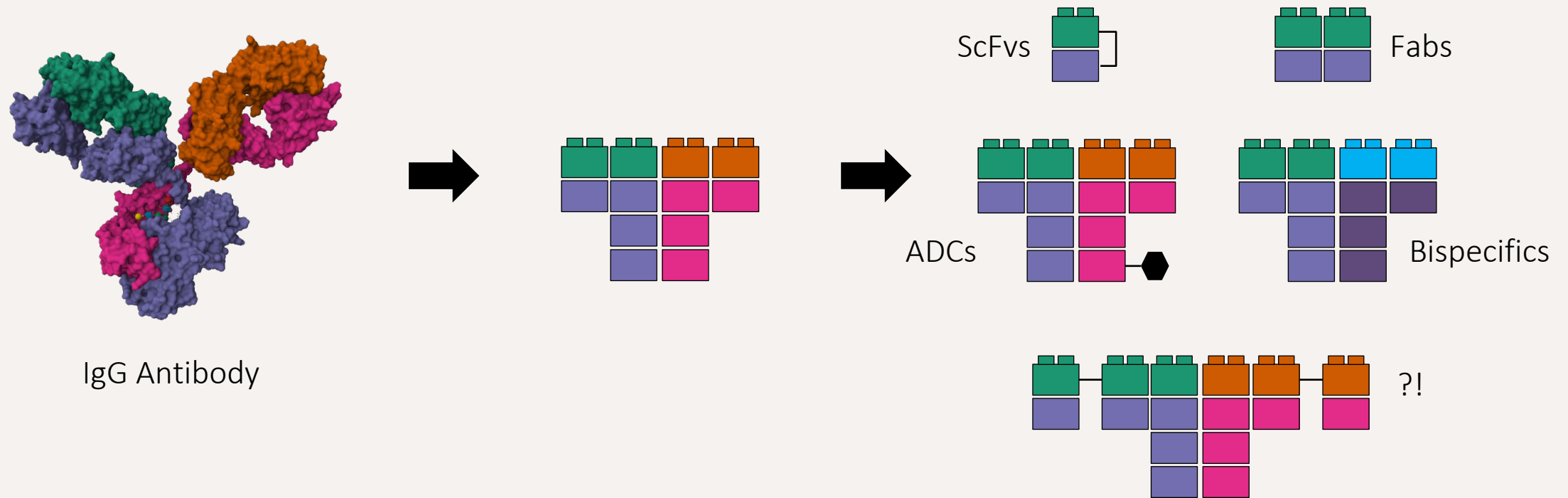
This evolution of therapeutic design
is being repeated across multiple entity classes

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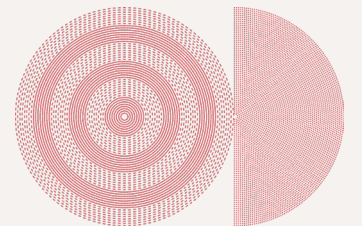
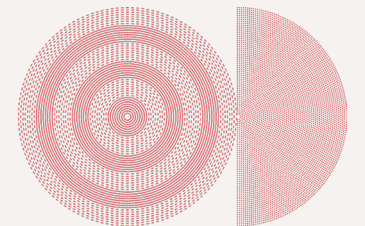# Examples of Complex Biological Therapeutics

Semaglutide, Novo Nordisk
Worldwide Sales 2024: $25.89B USD
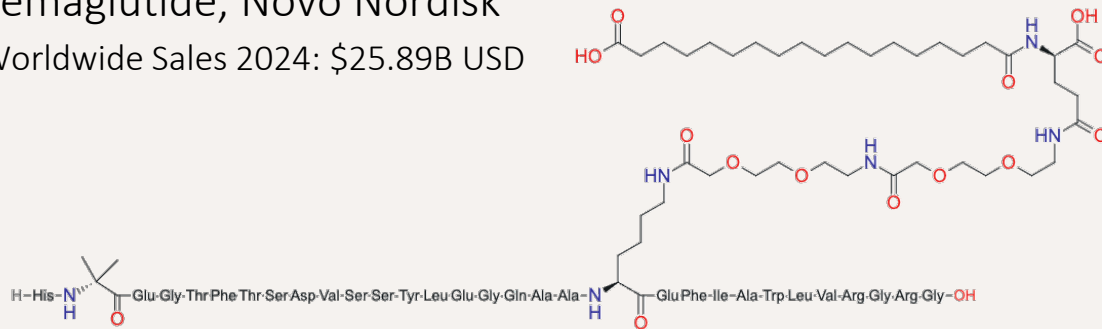
Kadcyla, Genentech
Worldwide Sales 2024: $2.32B USD
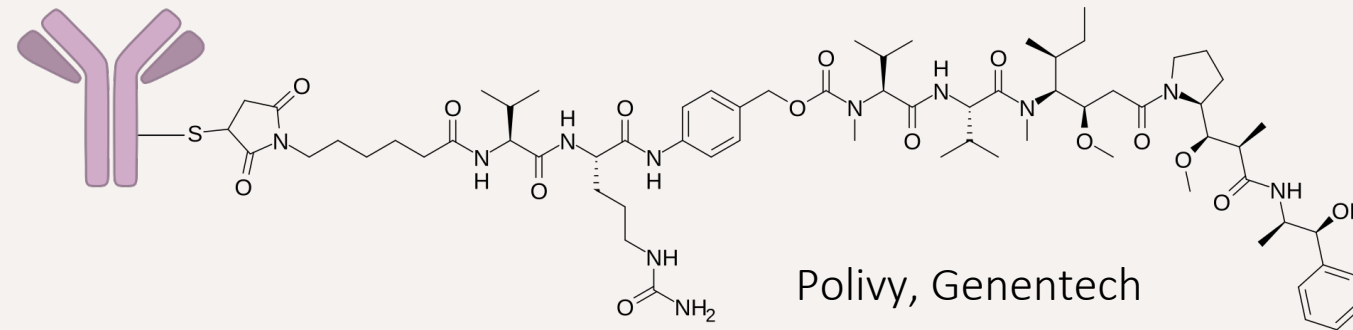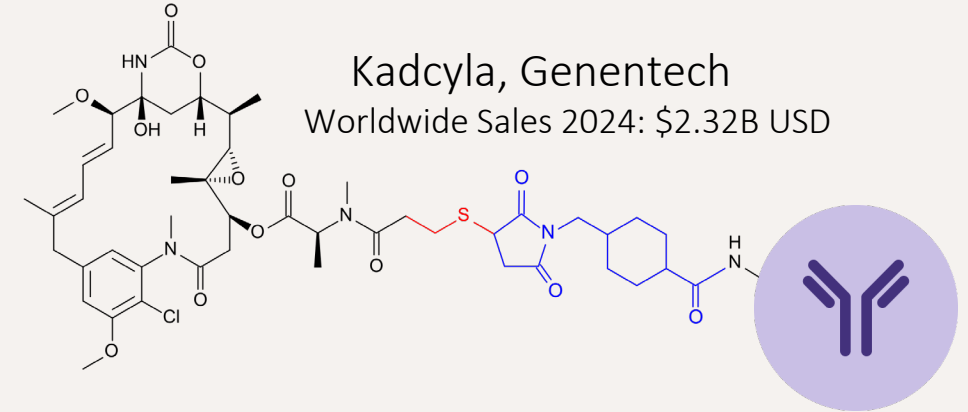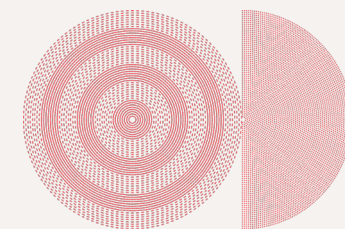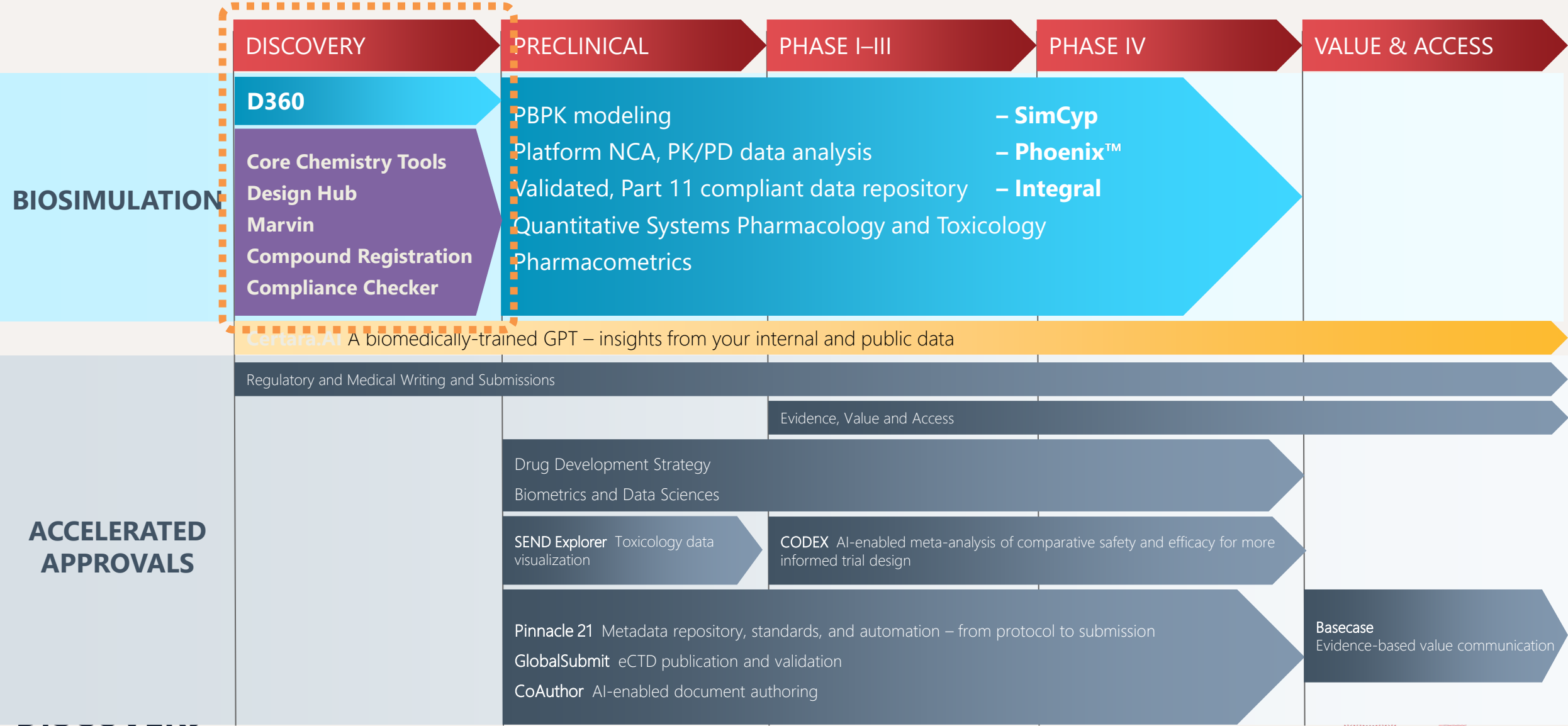
Polivy, Genentech
Worldwide Sales 2024: $1.30B USD

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Chemaxon's Plan

CERTARA

Is now a part of

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DISCOVERY

Combined Portfolio

DISCOVERY	PRECLINICAL	PHASE I–III	PHASE IV	VALUE & ACCESS

BIOSIMULATION

D360

Core Chemistry Tools
Design Hub
Marvin
Compound Registration
Compliance Checker

PBPK modeling   **– SimCyp**
Platform NCA, PK/PD data analysis   **– Phoenix™**
Validated, Part 11 compliant data repository   **– Integral**
Quantitative Systems Pharmacology and Toxicology
Pharmacometrics

Certara.AI A biomedically-trained GPT – insights from your internal and public data

ACCELERATED APPROVALS

Regulatory and Medical Writing and Submissions

Evidence, Value and Access

Drug Development Strategy
Biometrics and Data Sciences

SEND Explorer Toxicology data visualization

CODEX AI-enabled meta-analysis of comparative safety and efficacy for more informed trial design

Pinnacle 21 Metadata repository, standards, and automation – from protocol to submission
GlobalSubmit eCTD publication and validation
CoAuthor AI-enabled document authoring

Basecase
Evidence-based value communication

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Chemaxon Core Science

Analysis & Design

Drawing
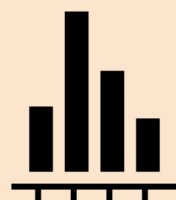
Calculators
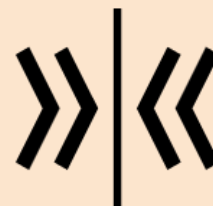
Standardization

Compliance

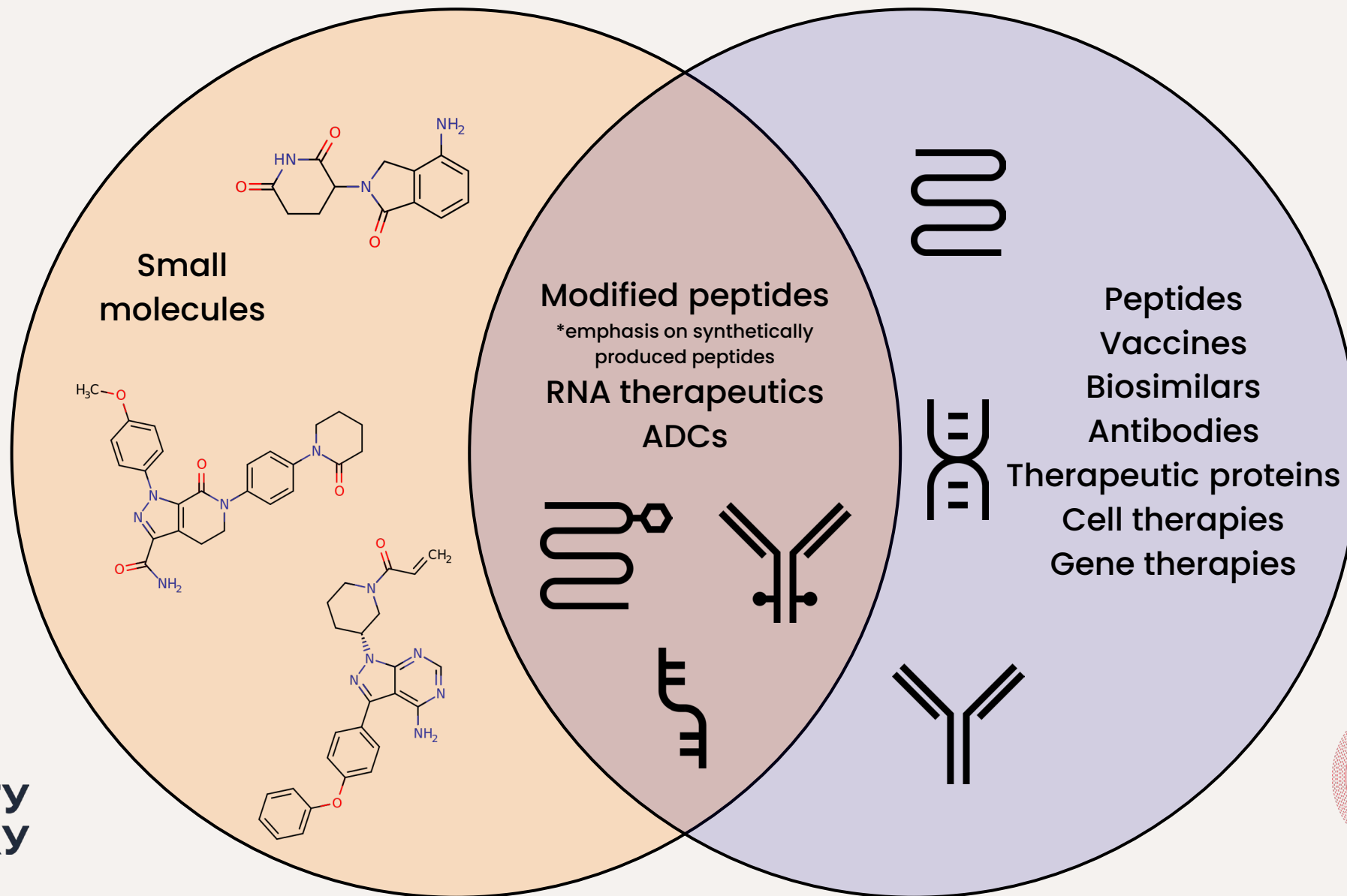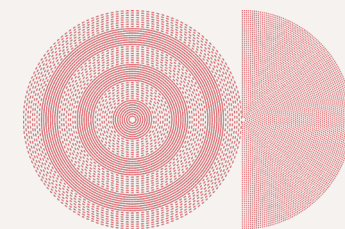Search

Registration

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13
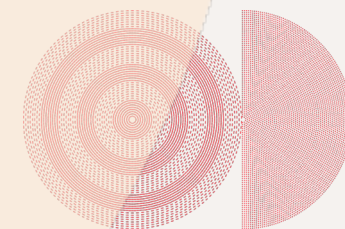
Support for Complex Drug Modalities

Small molecules

Modified peptides
emphasis on synthetically produced peptides
RNA therapeutics
ADCs

Peptides
Vaccines
Biosimilars
Antibodies
Therapeutic proteins
Cell therapies
Gene therapies

Working with Complex Modalities

How can we reliably **Represent**, **Share** and **Compare** complex modalities across our business processes?

HXEGTFTSDVSSYLEGQAAXEFIAWLVRGRG

Sequence View

Chemical View

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Working with Complex Modalities

Representation is Key

- Newer formats like HELM (and more recently BILN) combine both these chemical and biological viewpoints
- However, many informatics systems still struggle to reliably interconvert, depict and compare these entities
- Entities are often separated in registration and other data systems

PEPTIDE1{H.Aib.E.G.T.F.T.S.D.V.S.S.Y.L.E.G.Q.A.A.K.E.F.I.A.W.L.V.R.G.R.G}
| CHEM1{[C18Diacid-γGlu-(AEEA)2]} $ PEPTIDE1,20:R2-CHEM1,1:R1

HELM View
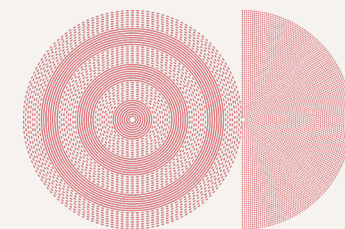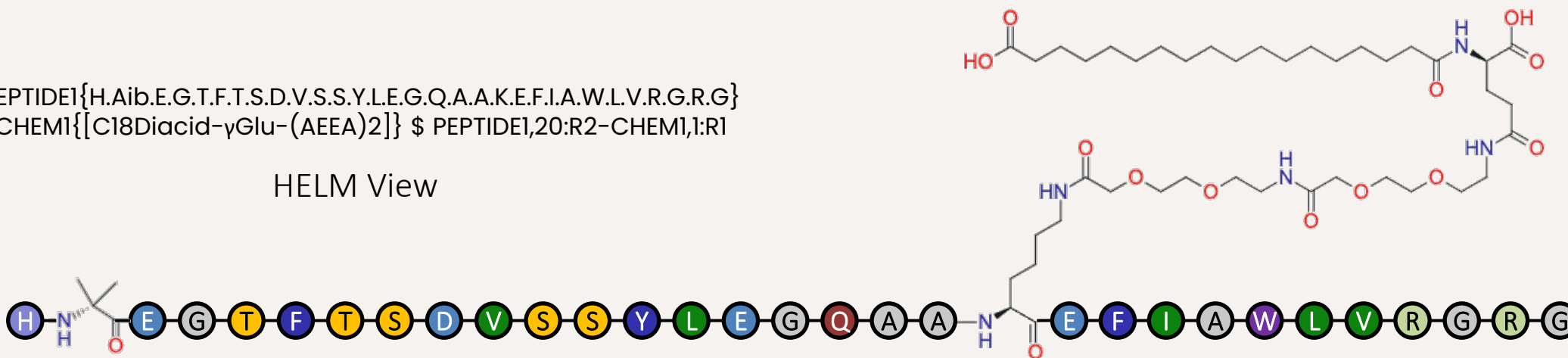
Working with Complex Modalities

Representation is Key
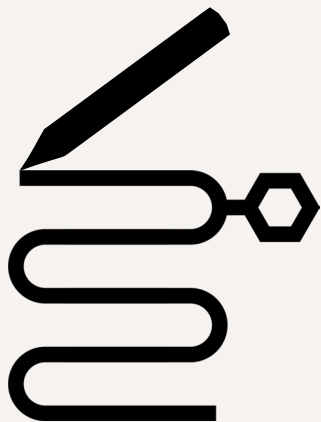
Draw
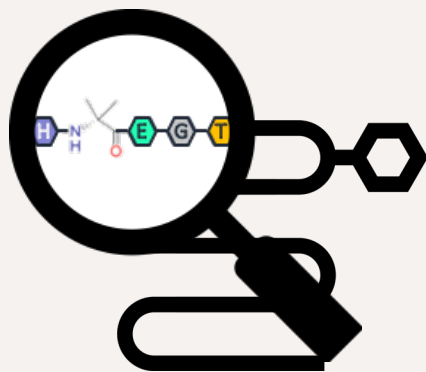
Depict

Search

Register

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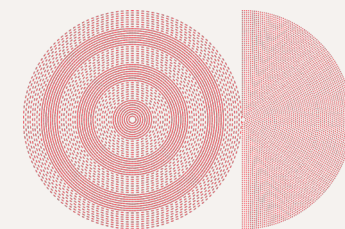
Taking our First Steps

Drawing and Depicting Biologics

Today: Basic peptide and monomer support

Representation

o   Structure-based only

Dictionary

o   Simple embedded AA monomer dictionary

Visualization

o   Switch between 1-letter and 3-letter code representation

o   View as residue or structure

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Note: Released Nov 2024
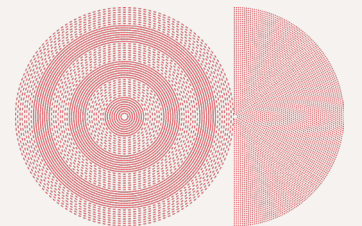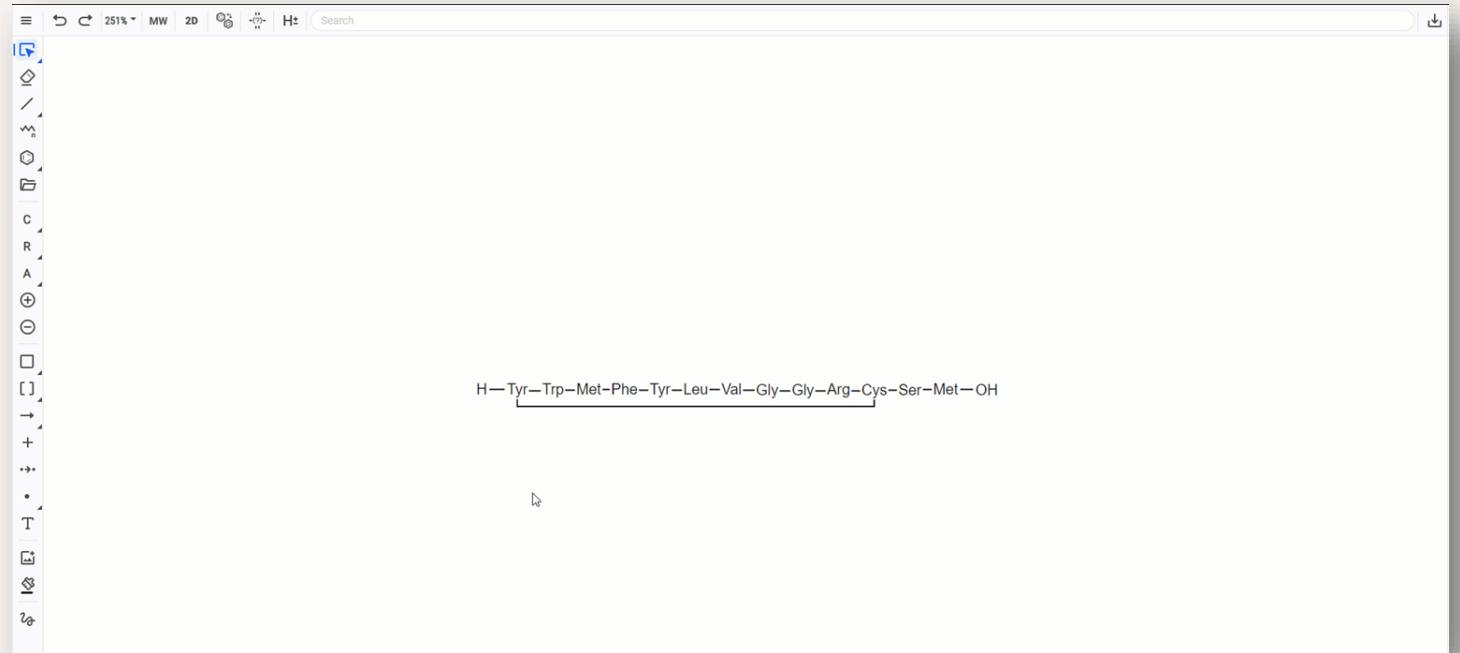
Drawing and Depicting Biologics

Planned: Monomer dictionary and HELM integration

Representation

- o HELM v2.0 notation support
- o Import and export support

Dictionary

- o Central monomer library
- o Accessed *via* Chemaxon Toolkits (Microservices)

Visualization

- o Monomer dictionary integration
- o 1-letter, 3-letter, custom IDs
- o Improved 2D clean support

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Note: Mockup for illustration purposes only

Registering Biologics

Today: Chemical registration of molecular entities

Representation

- o Structure-based

- o Up to 100M structures

Dictionary

- o No monomer dictionary

Registration

- o Chemical-based workflow

- o Support for custom registration fields

- o Supports peptides up to 200 AAs
  or RNA/DNA up to 70 NAs

Registering Biologics

Planned: Chemical registration of molecular entities

Representation

- Next: Sequence and HELM support
- Future: Complex modality support

Dictionary

- Central monomer dictionary
- Accessed *via* Chemaxon Toolkits (Microservices)

Registration

- Next: Chemical- and HELM-based workflows
- Next: Custom monomer registration
- Future: Complex modality registration

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Note: Mockup for illustration purposes only

Searching Biologics

Exploration: Identify Industry Needs and How these vary across Entity Types

PEPTIDE1{H.Aib.E.G.T.F.T.S.D.V.S.S.Y.L.E.G.Q.A.A.K.E.F.I.A.W.L.V.R.G.R.G}
| CHEM1{[C18Diacid-γGlu-(AEEA)2]} $ PEPTIDE1,20:R2-CHEM1,1:R1

HELM Object

Chemical Search

- o   Today: Exact, Substructure and Similarity searching of chemical structures

- o   Next: Convert small biologic HELM to chemical structure

Monomer Search

- o   Future: Exact, Substructure and Similarity searching of the central monomer dictionary
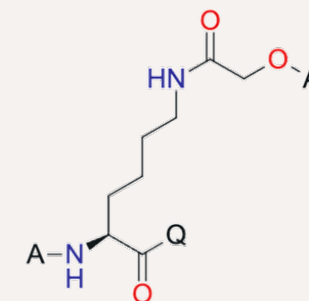
Sequence Search

- o   Future: Explore eg. BioJava and other open-source options

HXEGTFTSDVSSYLEGQAAXEFIAWLVRGRG

Sequence Search

Chemical Search

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Timeline *
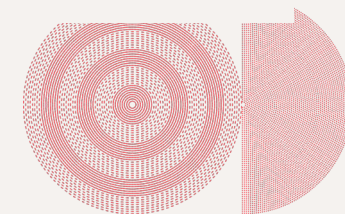
|	Next	Later	Future
Toolkits	• Monomer Dictionary • HELM string support • Peptide 2D clean	• BILN handling	• Monomer search • Sequence search
Marvin	• Peptide handling • Monomer dictionary • HELM editor	• Nucleic acid handling	
Compound Registration	• Marvin integration	• Monomer registration • HELM: Synthetic biologics registration	• Small Biologics registration • Complex conjugate registration

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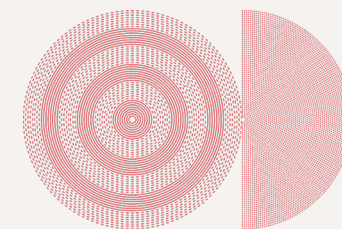
Looking Even Further Out

What about Biologics Design?

This is a very broad area!

But there are things that we could do in conjunction with our colleagues in D360 and Simcyp Discovery

**Integrate Biologics Design into the DMTA workflow**

- o Sequence alignment
  - - E.g., sequence aligned views of lead molecules
- o Calculate druglike molecular properties
  - - Either monomer-based or whole molecule?
- o SAR and MMP-style drill-downs
  - - E.g., monomer-oriented sequence comparisons?

Reference CHEMBL402482 Alignment: Similarity Matrix - All									Details
Sequence Alignment: Main									
	1	2	3	4	5	6	7	8	9
CHEMBL402482	I	L	W	Q	V	P	F	S	V
CHEMBL412034	I	L	F	Q	V	P	F	S	V
CHEMBL440266	I	L	Y	Q	V	P	F	S	V
CHEMBL216217	I	T	W	Q	V	P	F	S	V
CHEMBL426344	I	L	D	Q	V	P	F	S	V
CHEMBL437514	I	L	M	Q	V	P	F	S	V
CHEMBL263600	I	L	S	Q	V	P	F	S	V
CHEMBL263685	I	L	A	Q	V	P	F		

150 of 150 Sequences Displayed   Zoom   Unfilter All   Copy Alignment   Extract to Spreadsheet

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Conversations with our customers would be very welcome!
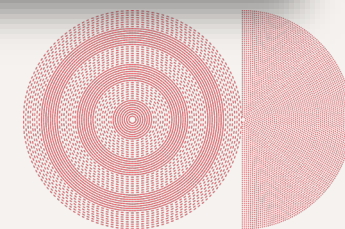
Our Goal

Enable customers to interchange information seamlessly between chemistry and biology entity representations

Thank You

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