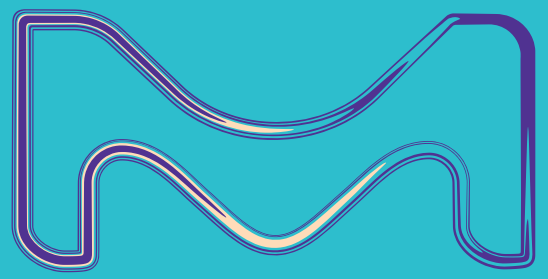
The biopharma business of Merck KGaA, Darmstadt, Germany operates as EMD Serono in the U.S. and Canada.

D360: unleash the power of data

Zhaowen Luo and Elke Hofmann



EMD SERONO

We are unique

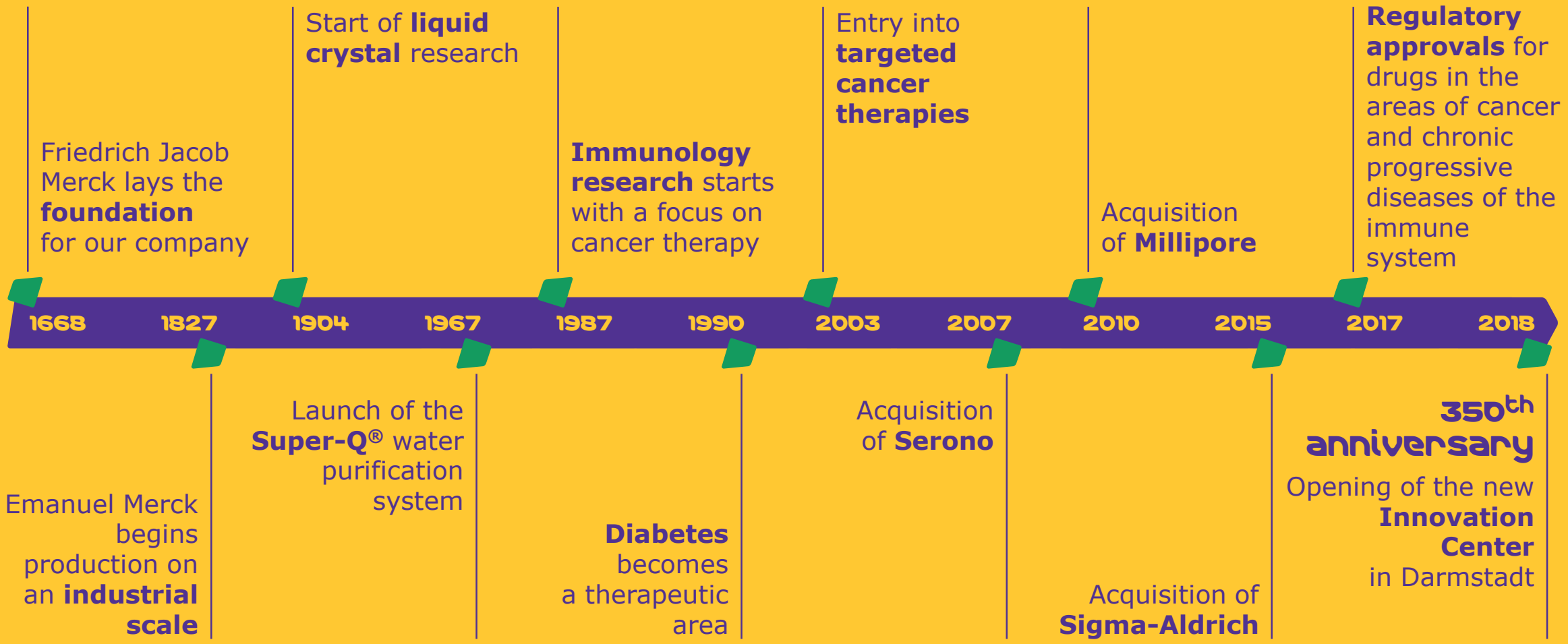
Since our founding 350 years ago, we've become truly global with more than **52,000 employees in 66 countries** working on break-through solutions and technologies.

Merck KGaA
Darmstadt, Germany

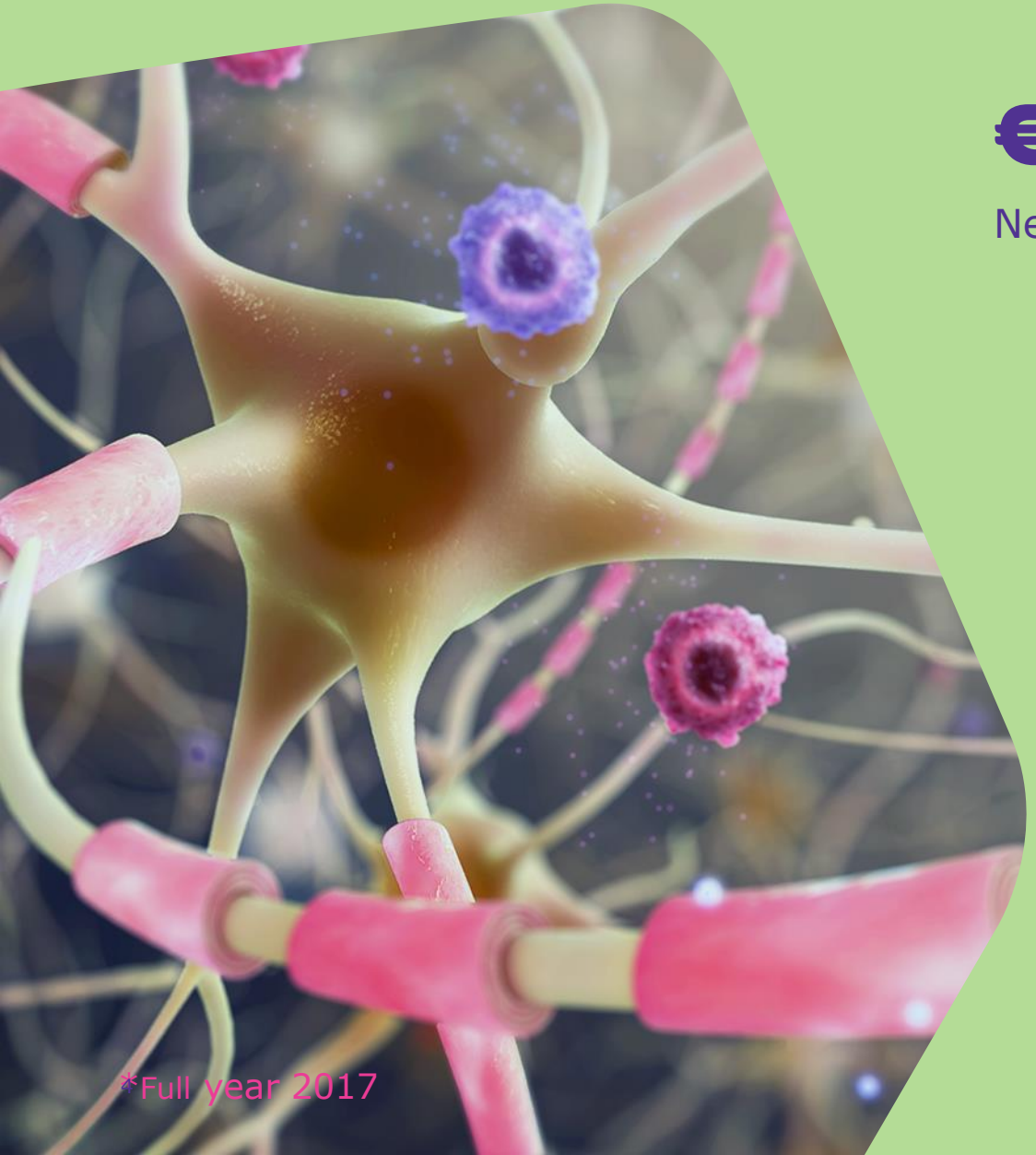
EMD Serono MilliporeSigma EMD Performance Materials

We are known as "Merck" internationally except for the United States and Canada, where we operate as EMD Serono in the biopharmaceutical business, MilliporeSigma in the life science business, and EMD Performance Materials in the high-tech materials business.

350 Years of curiosity



Learn more



€6.9bn

Net sales

46%

Share of Group Net Sales

20,000

Employees

€1.6bn

R&D spending

*Full year 2017

More Info

development pipeline

February 15, 2018

Phase I

M2698
p70S6K & Akt inhibitor
Solid tumors

M3814
DNA-PK inhibitor
Solid tumors

M9831 (VX-984)
DNA-PK inhibitor
Solid tumors

M6620 (VX-970)
ATR inhibitor
Solid tumors

M4344 (VX-803)
ATR inhibitor
Solid tumors

M3541
ATM inhibitor
Solid tumors

M8891
MetAP2 inhibitor
Solid tumors

M7583
BTK inhibitor
Hematological malignancies

avelumab
anti-PD-L1 mAb
Solid tumors

avelumab
anti-PD-L1 mAb
Hematological malignancies

M9241 (NHS-IL12)[2]
Cancer immunotherapy
Solid tumors

M7824
anti-PD-L1/TGFbeta trap
Solid tumors

M4112
Cancer immunotherapy
Solid tumors

M1095 (ALX-0761)[3]
anti-IL-17 A/F nanobody
Psoriasis

M6495
anti-ADAMTS-5 nanobody
Osteoarthritis

M5717
PeEF2 inhibitor
Malaria

Phase II

tepotinib
c-Met kinase inhibitor
Non-small cell lung cancer

tepotinib
c-Met kinase inhibitor
Hepatocellular cancer

avelumab - anti-PD-L1 mAb
Merkel cell cancer 1L[1]

sprifermin
fibroblast growth factor 18
Osteoarthritis

atacicept
anti-Blys/anti-APRIL fusion protein
Systemic lupus erythematosus

atacicept
anti-Blys/anti-APRIL fusion protein
IgA nephropathy

abituzumab
anti-CD51 mAb
Systemic sclerosis with interstitial lung disease

evobrutinib
BTK inhibitor
Rheumatoid arthritis

evobrutinib
BTK inhibitor
Systemic lupus erythematosus

evobrutinib
BTK inhibitor
Multiple sclerosis

Phase III

avelumab - anti-PD-L1 mAb
Non-small cell lung cancer 1L[1]

avelumab - anti-PD-L1 mAb
Gastric cancer 1L-M[1M]

avelumab - anti-PD-L1 mAb
Ovarian cancer platinum resistant/refractory

avelumab - anti-PD-L1 mAb
Ovarian cancer 1L[1]

avelumab - anti-PD-L1 mAb
Urothelial cancer 1L-M[1M]

avelumab - anti-PD-L1 mAb
Renal cell cancer 1L[1]

avelumab - anti-PD-L1 mAb
Locally advanced head and neck cancer

Registration

cladribine tablets
lymphocyte targeting agent
Relapsing multiple sclerosis[4]

- Oncology
- Immuno-Oncology
- Immunology
- Neurology
- General Medicine

[1] First-Line treatment; [1M] First-Line maintenance treatment.

[2] Sponsored by the National Cancer Institute (USA).

[3] As announced on March 30, 2017, in an agreement with Avillion, anti-IL-17 A/F nanobody will be developed by Avillion for plaque psoriasis and commercialized by EMDSerono.

[4] As announced on August 25, 2017, the European Commission has granted marketing authorization for cladribine tablets for the treatment of highly active relapsing multiple sclerosis in the 28 countries of the European Union in addition to Norway, Liechtenstein and Iceland.

Pipeline products are under clinical investigation and have not been proven to be safe and effective. There is no guarantee any product will be approved in the sought-after indication.

Research Informatics
Who we are and what we do

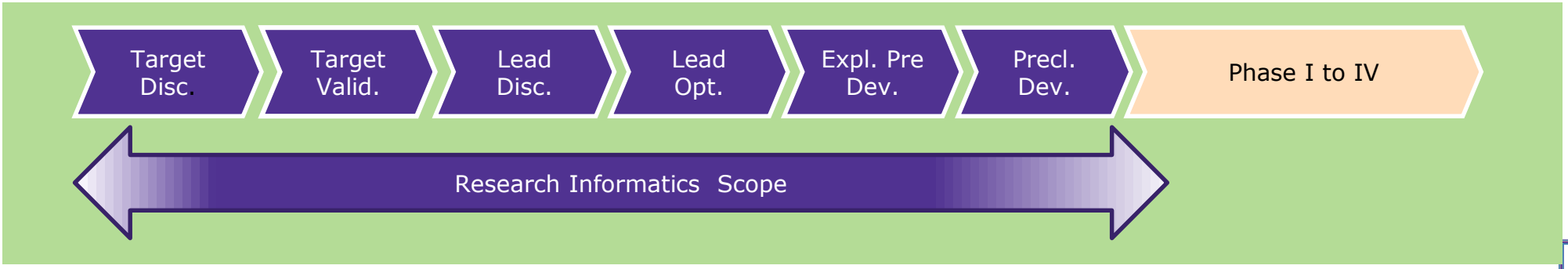
Research Informatics is part of the R&D Organization within Healthcare > Prescription Drugs

High-level RI objectives

- Enable data driven decision making by providing state-of-the-art research knowledge management
- Manage research data from internal & external sources
  - data capture
  - processing and analysis
  - integration
  - visualization

Our Mission:

- Enable project teams and R&D activities by providing state of the art scientific informatics solutions and bioinformatics project contributions



A brief History of SAR

1990s

- Pre-aggregated SAR values according to internal rules
- Available in Retrieval tool

Not optimal for SAR Analysis

2011

- Evaluation and implementation of dedicated SAR tool besides the Retrieval tool
- SAR aggregation rules not hundred percent compatible with internal rules, but acceptable

1st Generation of SAR Analysis

2016

- Different tools for Retrieval and SAR
- Both tools at the end of their life cycle
- Application survey
  - clearly pointed out dissatisfaction
  - Request to reduce number of tools

Start of project „New Retrieval and SAR Tool"

2017

- Evaluation with emphasis on
  - Software quality
  - Stability
  - Compatibility of aggregation rules
- Strongly driven by key users
- One solution for NCE drug discovery

Decision for D360

2018 .....

- Implementation
  - Data layer
  - Workspaces
  - Forms and templates
  - Visualizations
- Rollout end of 2018
- 2019 and beyond: extensions

So far: Good acceptance, High satisfaction rate

The Project „New Retrieval and SAR Tool“ for Small Molecules

Main requirements

- Seamless integration of Retrieval and SAR functionality in one application
- Global usage
- Good collaboration support (both internal and external)
- Potential to become an integrated Discovery Platform

Pre-determined Timelines

Feb 2017	Market assessment to identify suitable candidates
March 2017	Request for Proposal (RfP) Several vendors were contacted and asked for detailed information about their systems
July 2017	In-House evaluation with the most promising candidates
Dec 2017	Decision for one of the candidates
Dec 2018	Rollout of the selected solution

in a nutshell

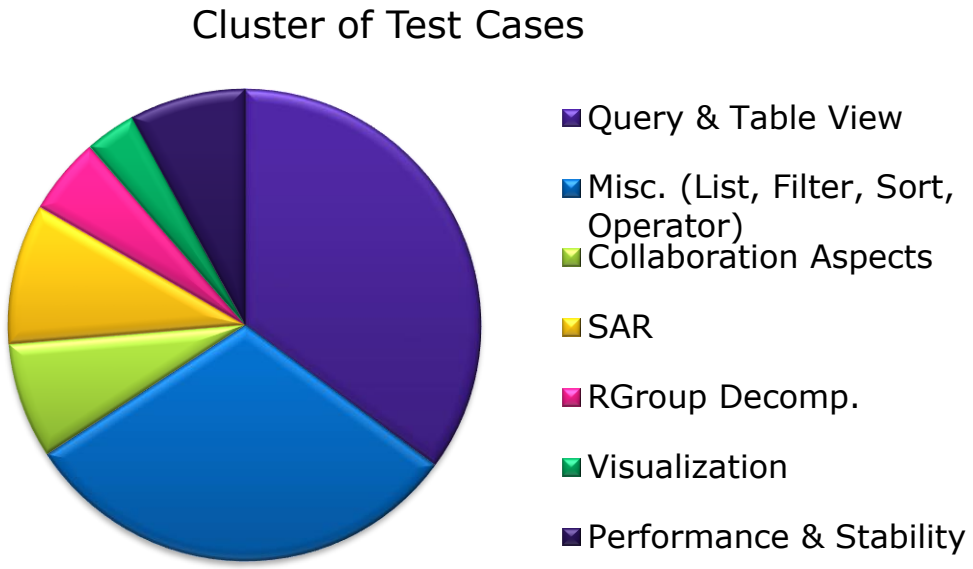
The Project - In-House Evaluation

Test cases

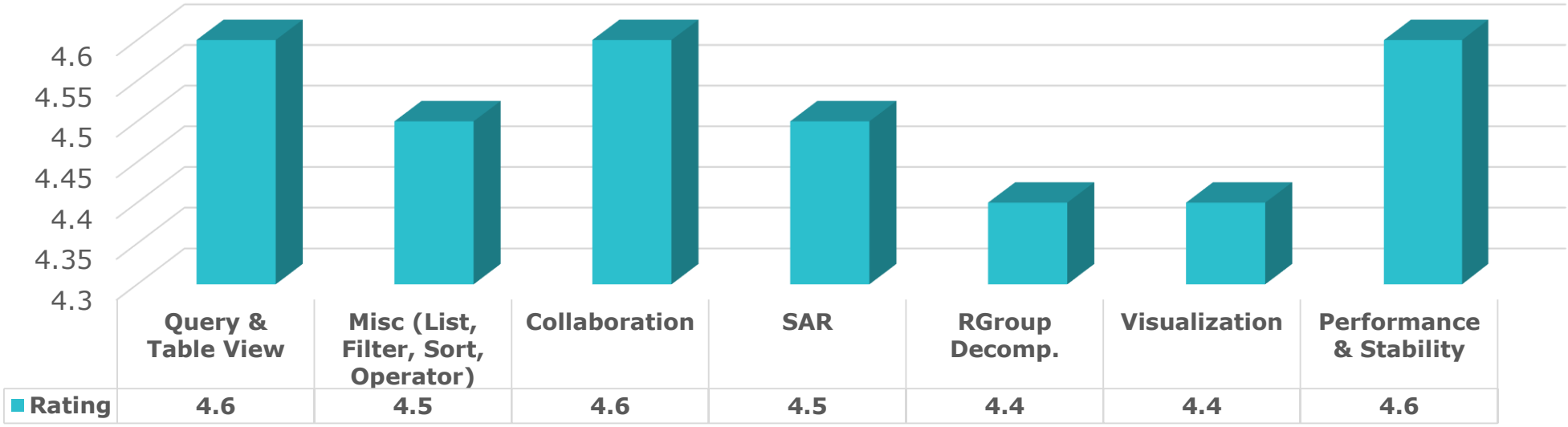
- Pre-defined test cases with different complexity
- Clustered in 7 categories

Engaged cross-functional Test Team

PoC for WebService integration



Feedback from Test Team: Rating for D360 (max 5)



	Query & Table View	Misc (List, Filter, Sort, Operator)	Collaboration	SAR	RGroup Decomp.	Visualization	Performance & Stability
Rating	4.6	4.5	4.6	4.5	4.4	4.4	4.6

The Project - Decision

D360 identified as next generation data retrieval and SAR tool

Based on

- In-house evaluation
  - Extensive training of key users
  - Approval from key users
- PoC integration of WebService
  - Confirmed by computational chemists
- Advisory service from independent consulting company *

* specialized and acknowledged for business and competitive intelligence services on research information systems for major pharmaceutical companies

The Project - Implementation

Implementation planned over 2 years

- Phase 1 – Laying the foundation
  - All Data needed to replace successor tools
  - Templates to cover different needs
  - Few WebServices
  - As much additional functionality as possible without endangering the timeline
  - ➢ Rollout in Dec 2018
- Phase 2 – exploring possibilities
  - Compound Design
  - Flexible platform to integrate additional chemo-informatic services
  - Combination screening data
  - Calculation server

Risk Analysis and Mitigation

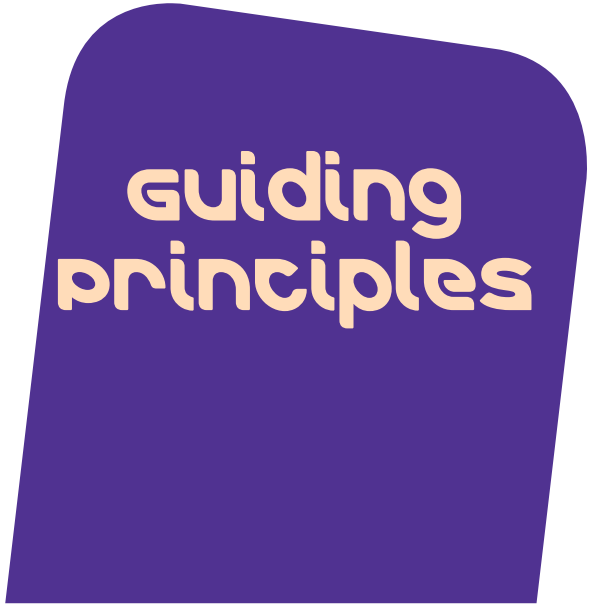
- Performance
  - Regularly check and optimization
  - Hypercare
- User Acceptance
  - Establish Key User Team to
    - ➢ Support introduction of D360, e.g. defining templates, giving input for training
    - ➢ Support other D360 user after roll-out
    - ➢ Enable project teams to quickly ease into D360
  - Intensive training
- Unrealistic expectation *
  - Involve Key User Team in planning of implementation phase 2 under consideration of cost/benefit ratio

* Examples:
  - One-stop solution – including self-serving docking, modelling
  - Implementation of convenience features which are rarely used

Data sharing and Transparency

Maximum data sharing

- All queries/templates/forms available for everyone
  - Project workspaces set to share with everyone
  - Personal workspaces encouraged to share
- Dedicated projects/functions workspace for project teams
- Examples and common templates
  - Dedicated “Template” workspace
  - Training workspaces – starting point for many users
- Annotations
  - Important feature to share knowledge inside project team



Maximum data availability

- Data Layer contains
  - Compounds (NCE)
  - Assay results as well as in-silico ones
  - Workflow information – assay requests
  - Logistics – availability of compounds
  - Documents
- Flexible data catalog in form of navigation tree
- Drill down to individual data point
- Virtual compounds – design workflow incorporated
- Computational server and virtual assays

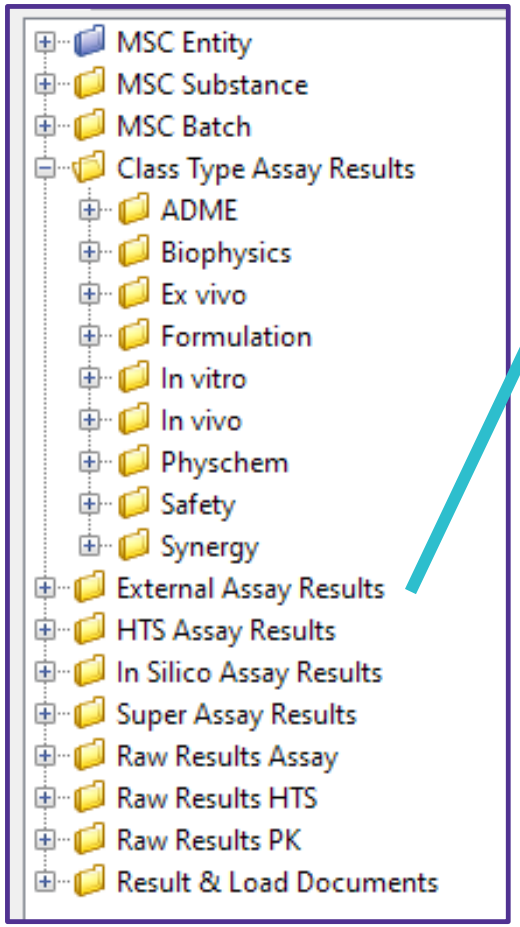
Data Catalogue

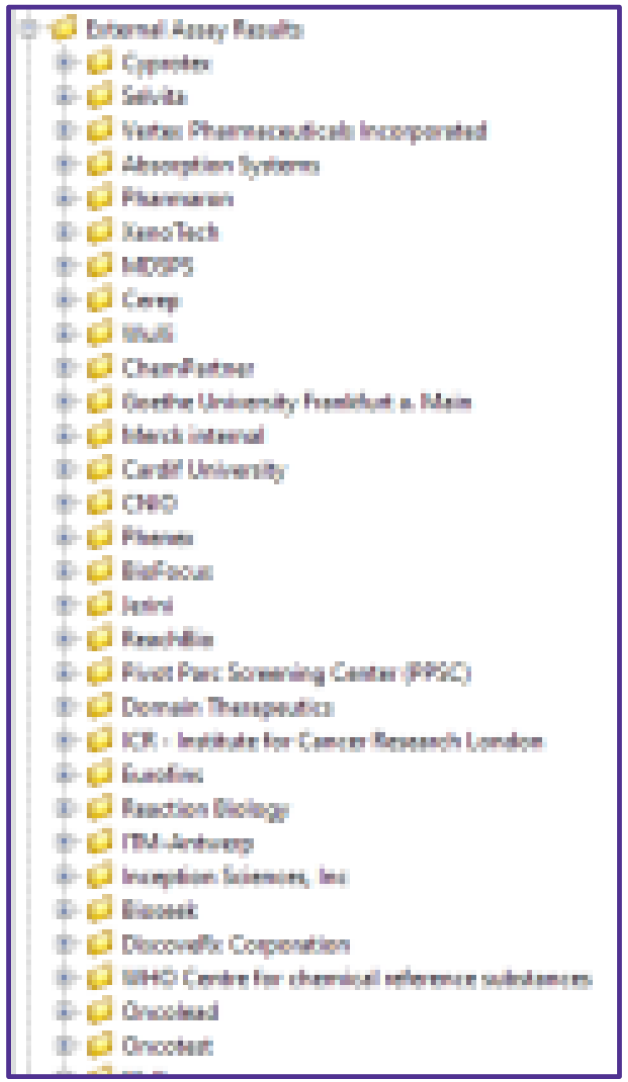
Compound – three levels

- **Entity**
- **Substance (Salt)**
- **Batch**

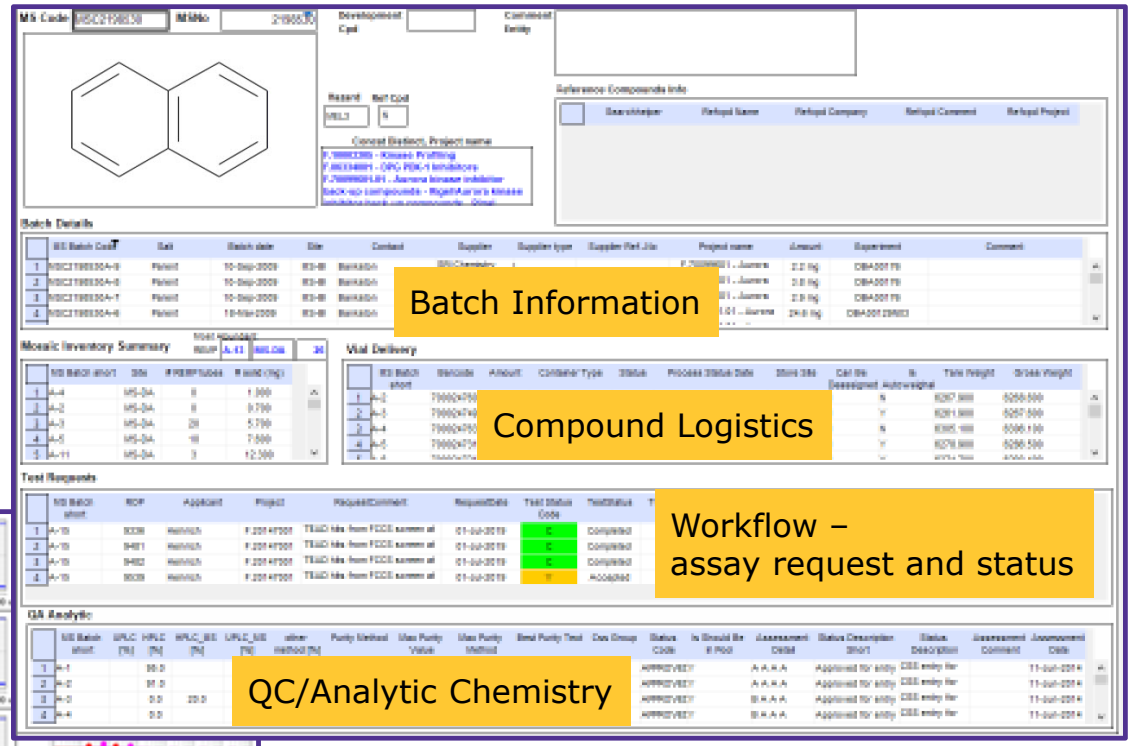
Assay Data – categorized to facilitate navigation

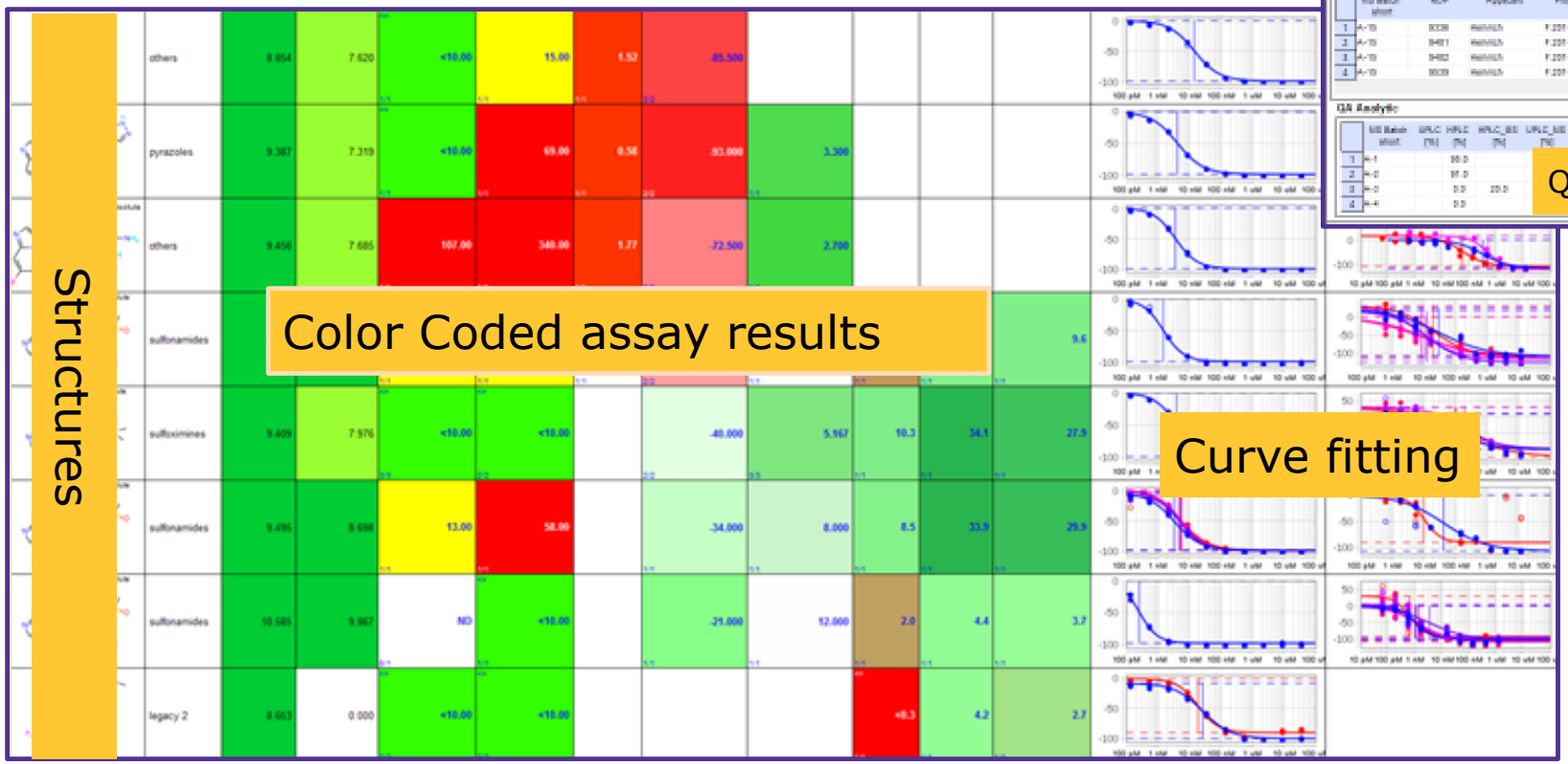
- **Classification of assays**
- **External suppliers**
- **HTS**
- **Super assays**
- **Raw result – form building**
- **Documents**





Different templates for different needs
SAR table - compound-centric form.

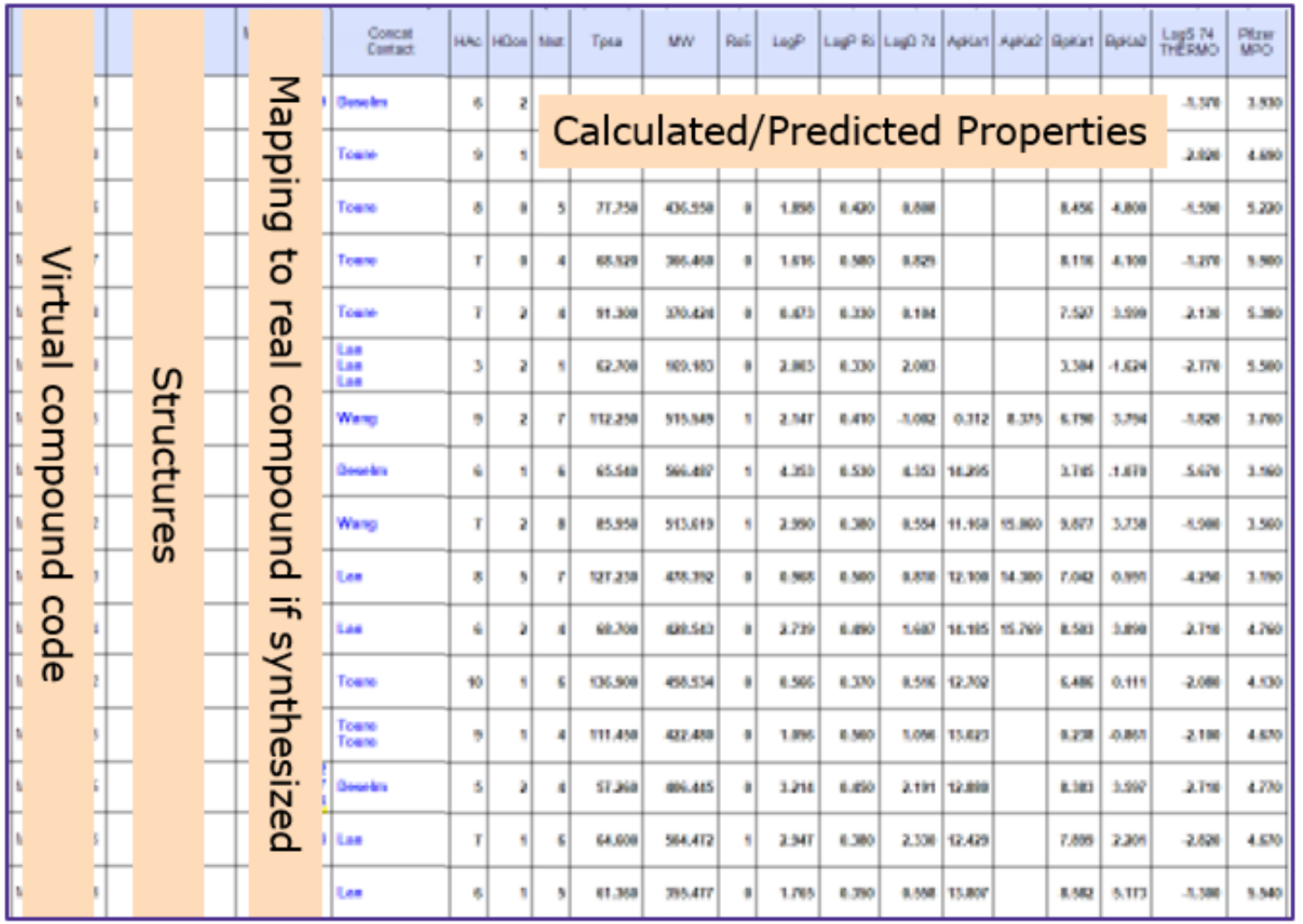




Compound Design Workflow

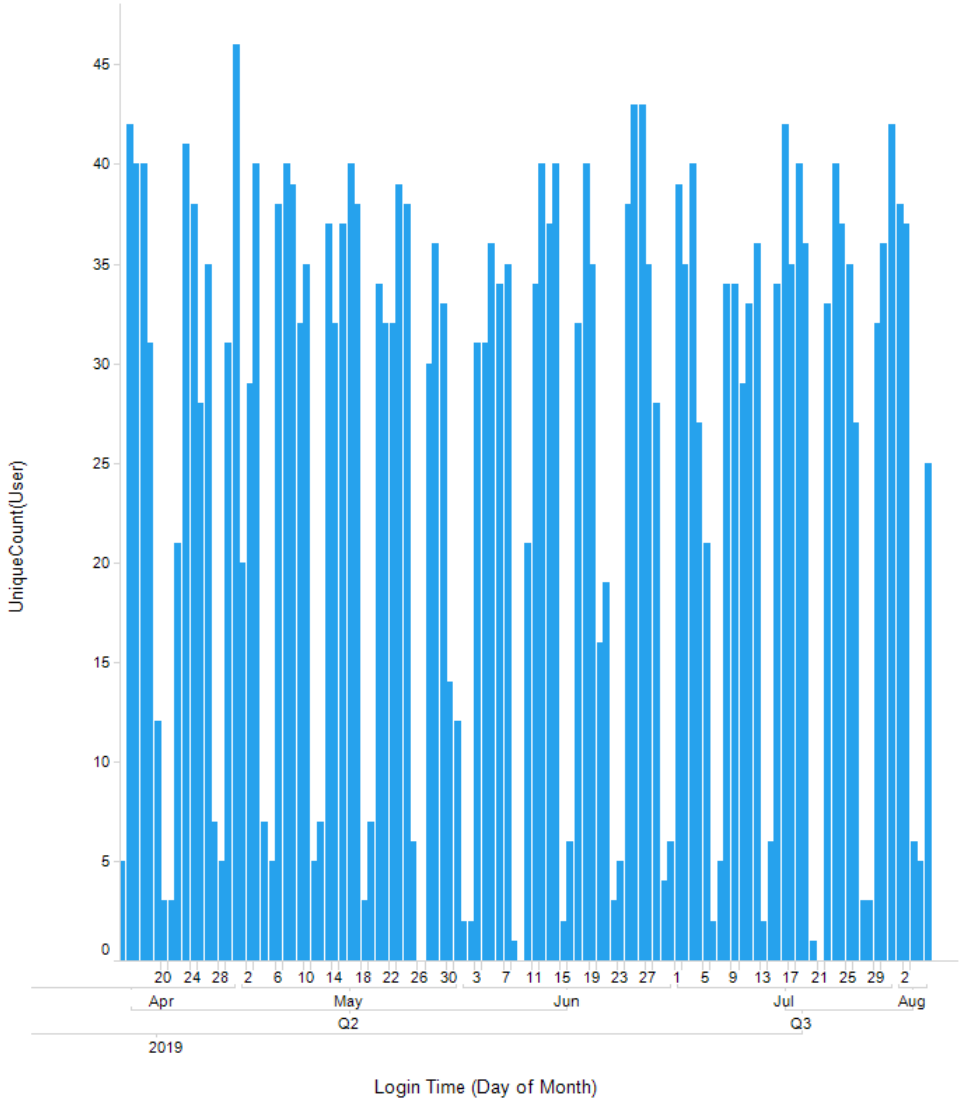
Most functions available in D360

- **Registration of virtual compounds is done in a separate system**
  - **Structure, scientific project, …**
- **D360 is used for Retrieval and SAR along real compounds**
  - **Pre-calculated PhysChem Properties**
  - **In silico assays**
  - **Status tracking**
    - **Rating**
    - **Synthesis Plan**
    - **Availability as real compound**



Statistics
A widely adopted platform

- ~ 185 active users
  - Very consistent daily usage (graph in the right)
- Over one third are frequent users (more than two or three times a week)
  - All medicinal chemists
  - Most computational chemists
  - Project teams
- > 1,300 templates created
  - Cover all NCE discovery projects
- > 15,000 annotations recorded



One platform for everyone (in NCE drug Discovery)

1

Chemists

- Data retrieval
- SAR analysis
- Hit and Lead Decisions

2

Designers

- Virtual compounds
- Property calculation
- Predictions

3

Biologists

- Data availability and QA
- Data integrity
- Data accuracy and completion

4

Others: pre-clinical development

- Compound fact sheet
- Coverage of data

Visibility of Data Details encourages Communication

Data Consumer – Medicinal Chemists

- Simple data for quick decision
  - Efficient decision making among thousand compounds
  - SAR: one assay, one value
  - Always have numeric value – coloring, sorting, visualization and comparison
- Ignore experimental errors
  - Ranking compounds in the error margin

Data Producer - Biologists

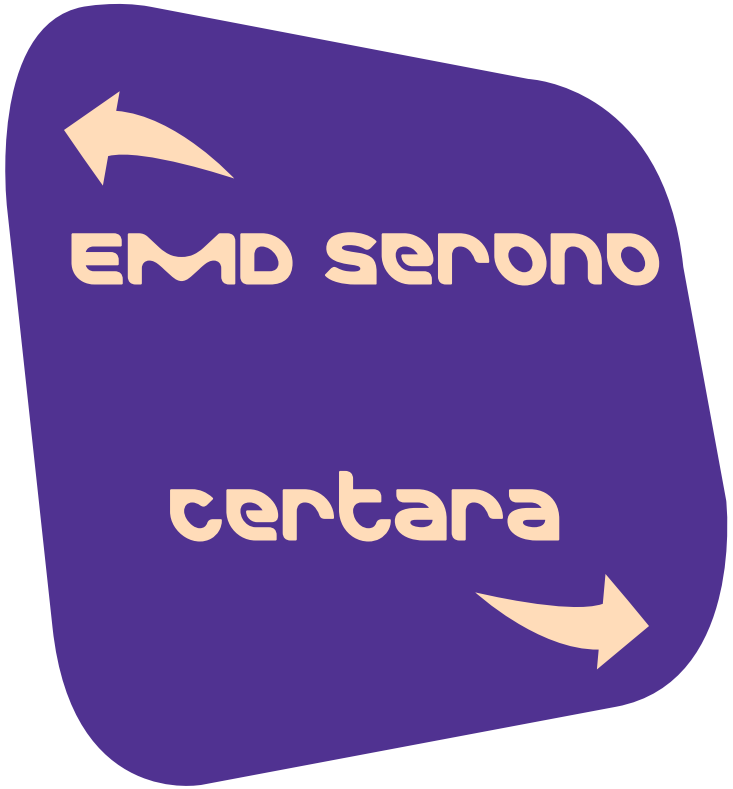
- Data accuracy
  - Numeric value not always available – can't compare in many cases
  - Review curves
  - Experiment and result comments equally important as results
- Data quality
  - Repetition of experimental data

1. Drill-down: aggregated data with drill-down to single data points
2. Extrapolated data under certain conditions – approved by screeners
3. Column orders – summary data first, and detail/comments last or even hidden

Acknowledgments

Elke Hofmann
Michael Hofmann
David Hand
Alexander Roberts
Michael Krug

Lars Burgdorf
Hans-Peter Buchstaller
Theresa Johnson
Lesley Liu-Bujalski
Srinivasa Karra
Andrea Unzue Lopez
Andreas Blum
Momar Toure
Constantin Neagu
Huijun Dong
Igor Mochalkin



Glenn Stucker
Fabian Rauscher
Dennis Powell
David Lowis
Ian Ingram
Mark Lee
Nina Hofle