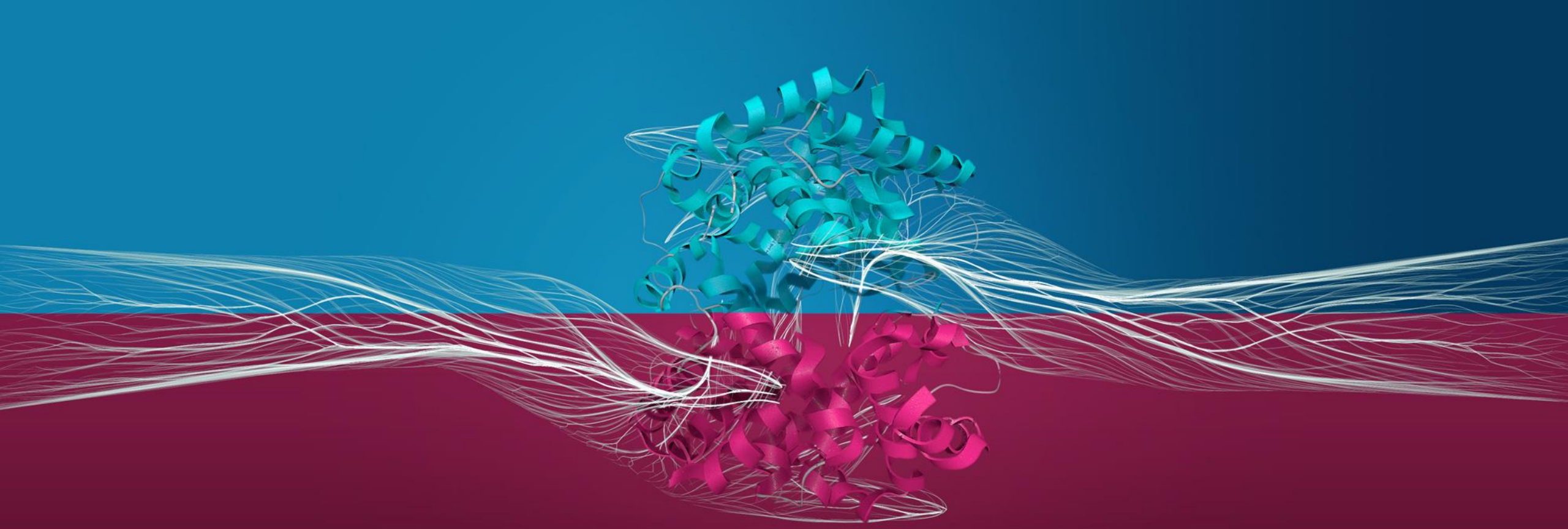


congruence TX

Driving Efficiency and Managing Change in Drug Discovery

KNIME Data Hop – May 15, 2025, Toronto

Corporate Highlights

Anticipate Initiation of Phase 1 Trial and Nomination of Two DCs in the Next 18 Months

Proprietary Pipeline Advancing Towards Clinic

First in Class/Best in Class Small Molecule Correctors for difficult-to-drug, genetically-validated targets, including:

- MC4R-Deficient Genetic Obesity
- GBA-Driven Parkinson's Disease
- Alpha-1 Antitrypsin Deficiency

Leading Discovery Platform and Product Engine

Computationally-Driven Design of Small Molecule Correctors to stabilize and rescue mutated proteins

Revenir™ uniquely enables Congruence to:

- Capture protein conformer landscapes
- Ascertain biophysical and thermodynamic properties of wildtype and mutant proteins
- Predict small molecules that rescue aberrant protein function

Well-Capitalized with Leading Investor Syndicate

Series A financing of **US$66 million** in Dec 2021 (extension Mar 2023 at same valuation) by leading institutional life science investors

Congruence is the first biotech company to set up a wet lab at Mila

Current Focus of Revenir™: **Pharmacological Correctors by Design**

Large, Well-Defined Opportunity

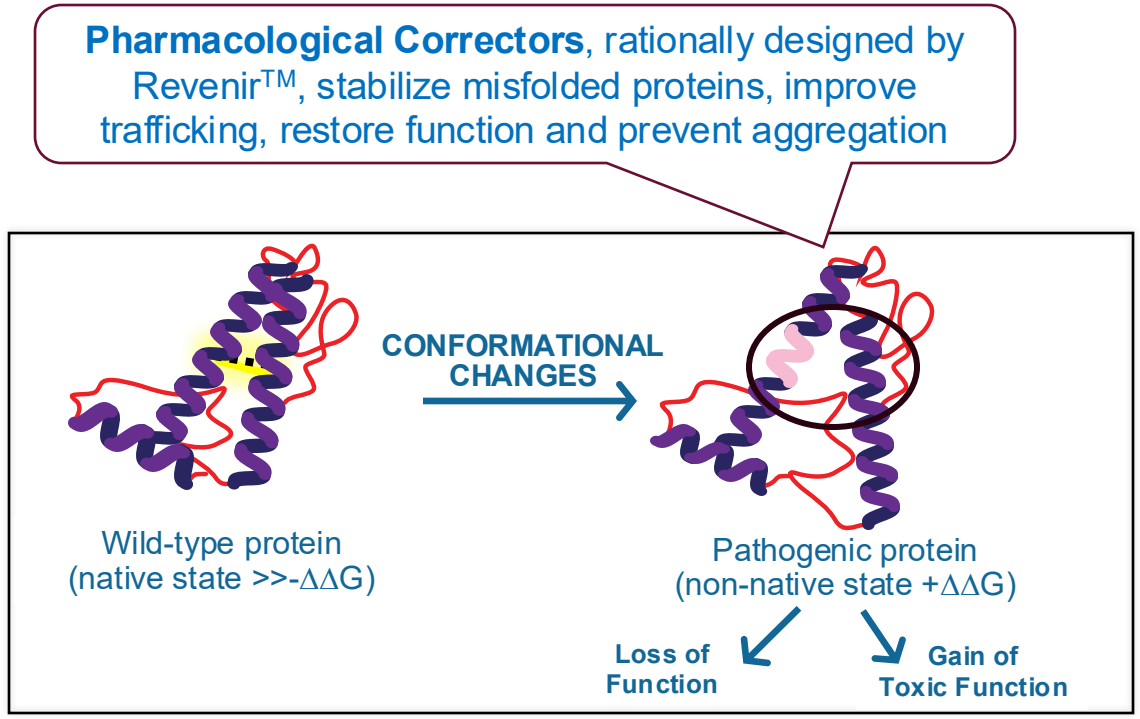
- Protein instability is the key defect in large number of diseases
- Rare, monogenic diseases of protein misfolding are severe examples along a spectrum of protein instability across the genome
- Protein instability leads to loss of function through **protein degradation** and mis-trafficking or gain of function through toxic aggregation

Pharmacological Correctors Have Achieved Significant Commercial Success

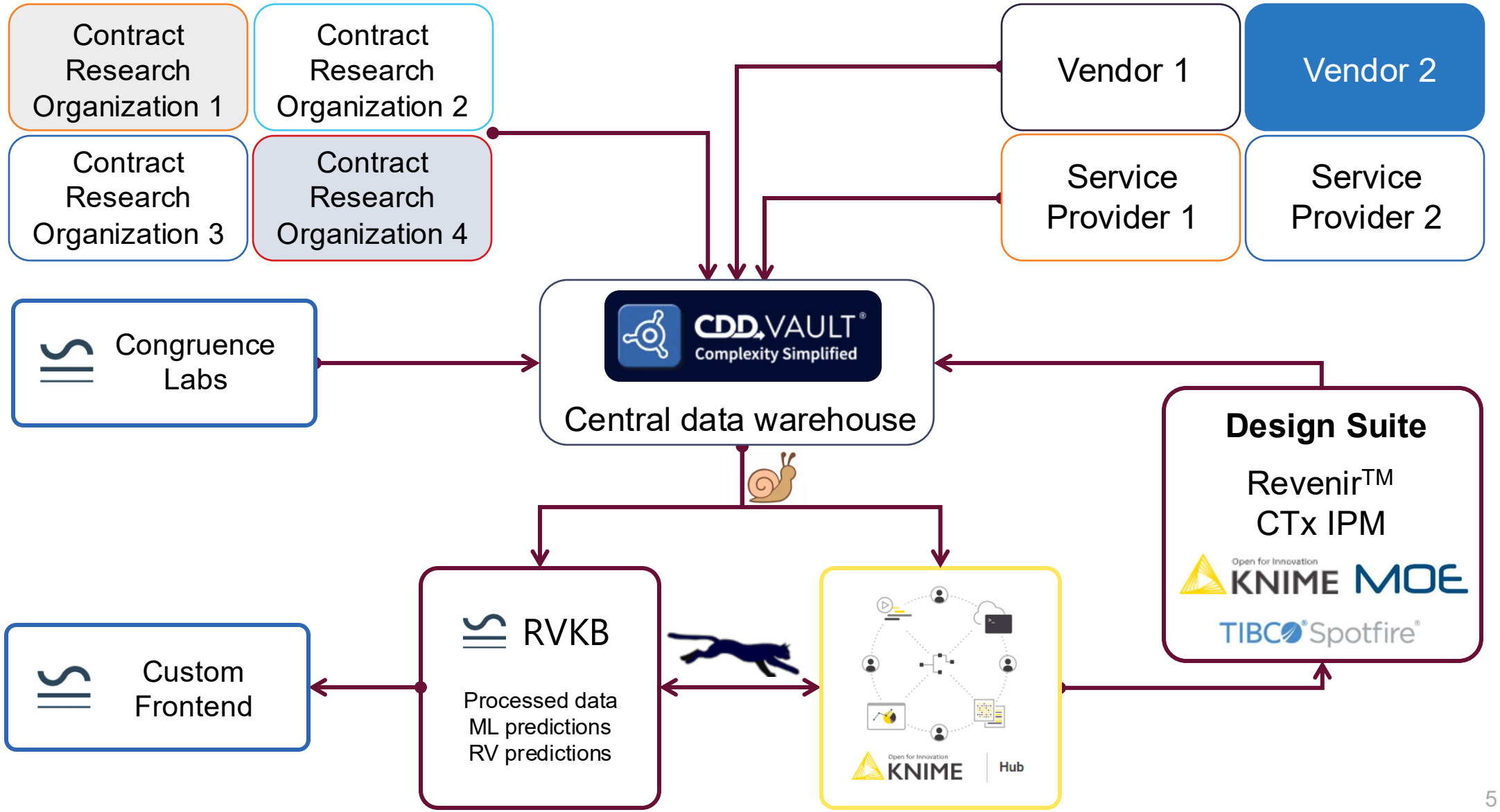
- Trikafta®, Vertex for cystic fibrosis with US sales ~ $8.9B
- Vyndaquel®, Pfizer/FoldRx for ATTR-CM with US sales ~ >$3.3B

Revenir Dramatically Improves Traditional Discovery Methods

- Revenir enhances efficiency and probability of success vs. traditional means (i.e. HTS) used to discover previous pharmacological correctors

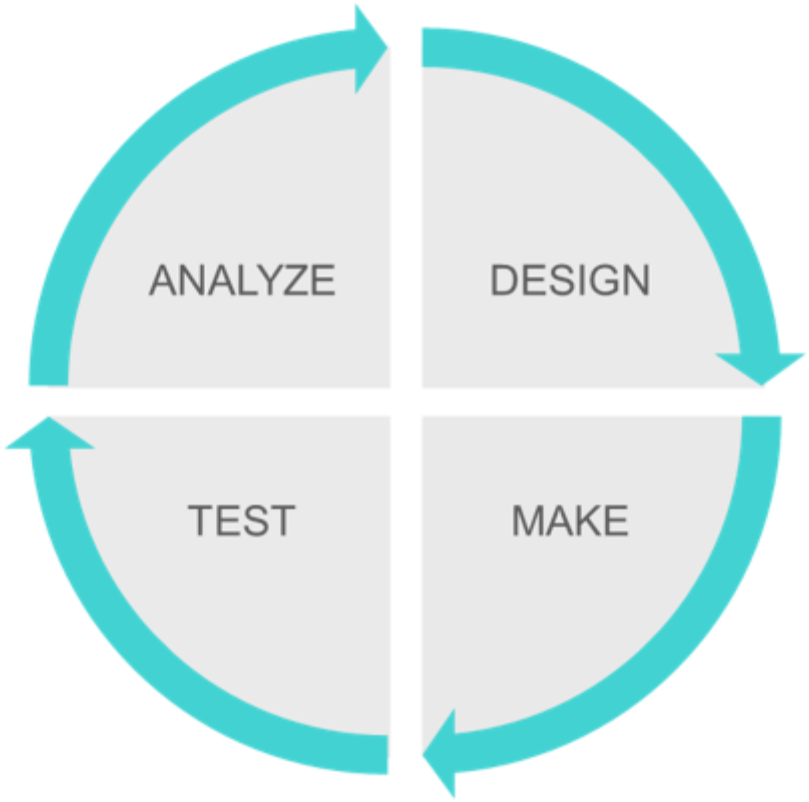


Example of how compound data flows in drug discovery



The central paradigm of lead optimization in drug discovery

NEW HYPOTHESIS GENERATION



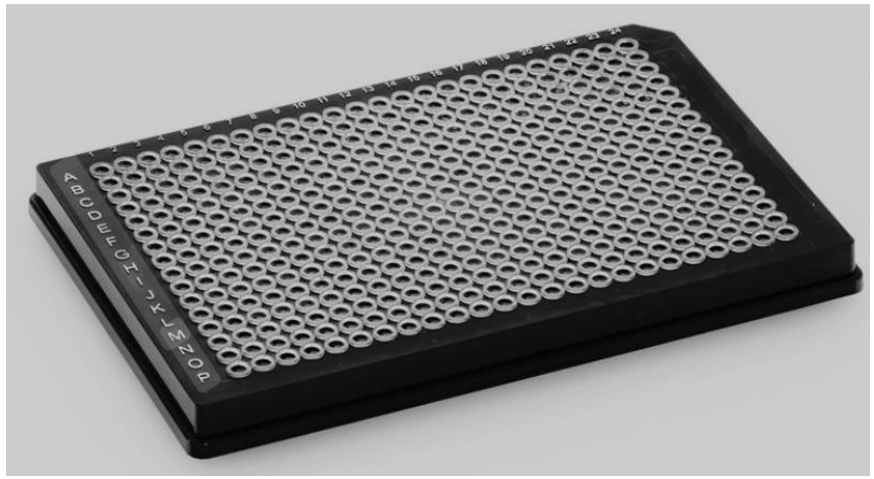
DESIGN MOLECULES TO TEST NEW HYPOTHESES

COLLECT DECISION DRIVING DATA EARLY

EFFECTIVELY DEPLOY CHEMISTRY RESOURCES

Deep dive today:
an example from the “wet lab” where we leveraged an opportunity to drive efficiency using KNIME

The need to analyze large volumes of data from biological assays provided an opportunity for process improvement with KNIME



384-well plate

- Each “well” contains a unique biological experiment

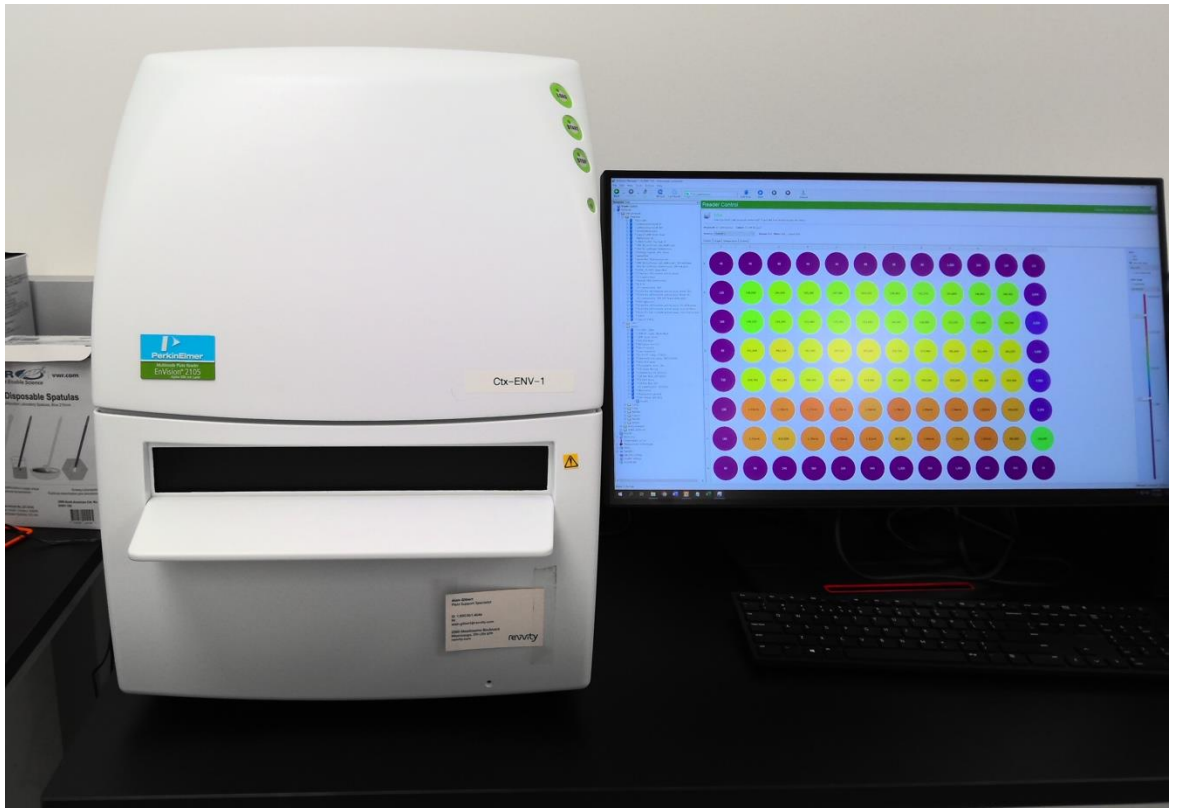


Plate reading instrument collects data related to the success of the biological experiment from each well

Data is exported from instrument and analyzed by assay scientists

Instrument reads data from 384-well plates and exports .csv files for further analysis

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
1	Plate information																								
2	Plate	Repeat	Barcode	Measured	Chamber t	Chamber t	Humidity a	Humidity a	Ambient te	Ambient te	Group	Label	ScanX	ScanY	Measinfo	Kinetics	Measurement date								
3	1	1		11.92	30.03	30.08	13.7	13.8	24.17	23.97	1		0	0		0									
4																									
5	Background information																								
6	Plate	Label	Result	Signal	Flashes/Ti	Meastime	MeasInfo																		
7	1		0	83	500	00:00.0																			
8																									
9	Results - channel 1 (RFU)																								
10		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
11	A	2467	1340	1667	1675	1879	1572	1720	1629	1817	1574	1689	1667	1676	1571	1609	1556	1660	1596	1650	1517	1786	1546	1699	1873
12	B	2384	2600	1681	1778	1648	1699	1727	1776	1642	2136	1649	1700	1630	1705	1619	1689	1699	1702	1703	1783	1756	1771	1669	1712
13	C	2435	2133	1754	1752	1771	1620	1710	1863	1758	1747	1789	1680	1766	1756	1721	1713	1824	1821	1793	1706	1762	1762	1761	1717
14	D	2244	2493	1766	1813	1717	1767	1662	1846	1826	1791	1693	1726	1673	1715	1623	1718	1679	1753	1744	1781	1725	1745	1755	1664
15	E	2306	2522	1872	1878	1837	1702	1947	1738	1739	1817	2041	1757	1753	1698	1736	1705	1797	1685	1885	1723	1840	3450	1783	1522
16	F	1558	1903	1700	1795	1707	1855	1740	1760	1817	1714	1785	1723	1757	1726	1738	1755	1726	1777	1659	4156	1737	1778	1675	1368
17	G	1781	1843	1779	1764	1798	1791	1848	1720	1755	1682	1771	1745	1750	1666	4479	1699	1703	1767	1751	1717	1766	1788	1802	1455
18	H	1729	1802	1704	1826	1821	1832	1774	1810	1823	1850	1661	1686	1749	1816	1701	1731	1857	1790	1720	1819	1752	1822	1827	1324
19	I	1801	1731	1985	1941	1909	1871	1882	1810	1924	1788	1745	1766	1786	1797	1784	1763	1761	1820	1806	1737	1777	1766	1814	1062
20	J	1678	2455	1841	1822	1819	1922	1749	1818	1821	1797	1813	1787	1788	1848	1715	1778	1739	1844	1781	1838	1790	1828	1704	675
21	K	1682	1786	1907	1888	1854	1769	1807	1856	1773	1730	1744	1795	1909	1868	1797	1821	1758	1821	1857	1782	1775	1743	1752	472
22	L	1536	1850	1763	1843	1830	1762	1788	1777	1803	1792	1807	1807	1733	1803	1901	1882	1815	1802	1739	1849	1798	1806	1735	697
23	M	2151	1767	1842	1751	1879	1712	1944	1750	1790	1709	1849	1709	1801	1806	1798	1818	1843	1775	1768	1768	1710	1751	1855	463
24	N	1665	1789	1865	1791	1809	1867	1835	1773	1738	1795	1725	1769	1679	1798	1814	1833	1771	1865	1801	1767	1713	1731	1758	519
25	O	1710	1694	1805	1732	1797	1725	1785	1758	1680	1648	1824	1691	1873	1802	1686	1717	1763	1658	1705	1664	1763	1695	1835	851
26	P	1487	1611	1667	1699	1666	1650	1591	1685	1648	1626	1650	1730	1619	1670	1687	1655	1654	1737	1711	1719	1670	1682	1654	1125
27																									

Restructuring of output file is required for analysis

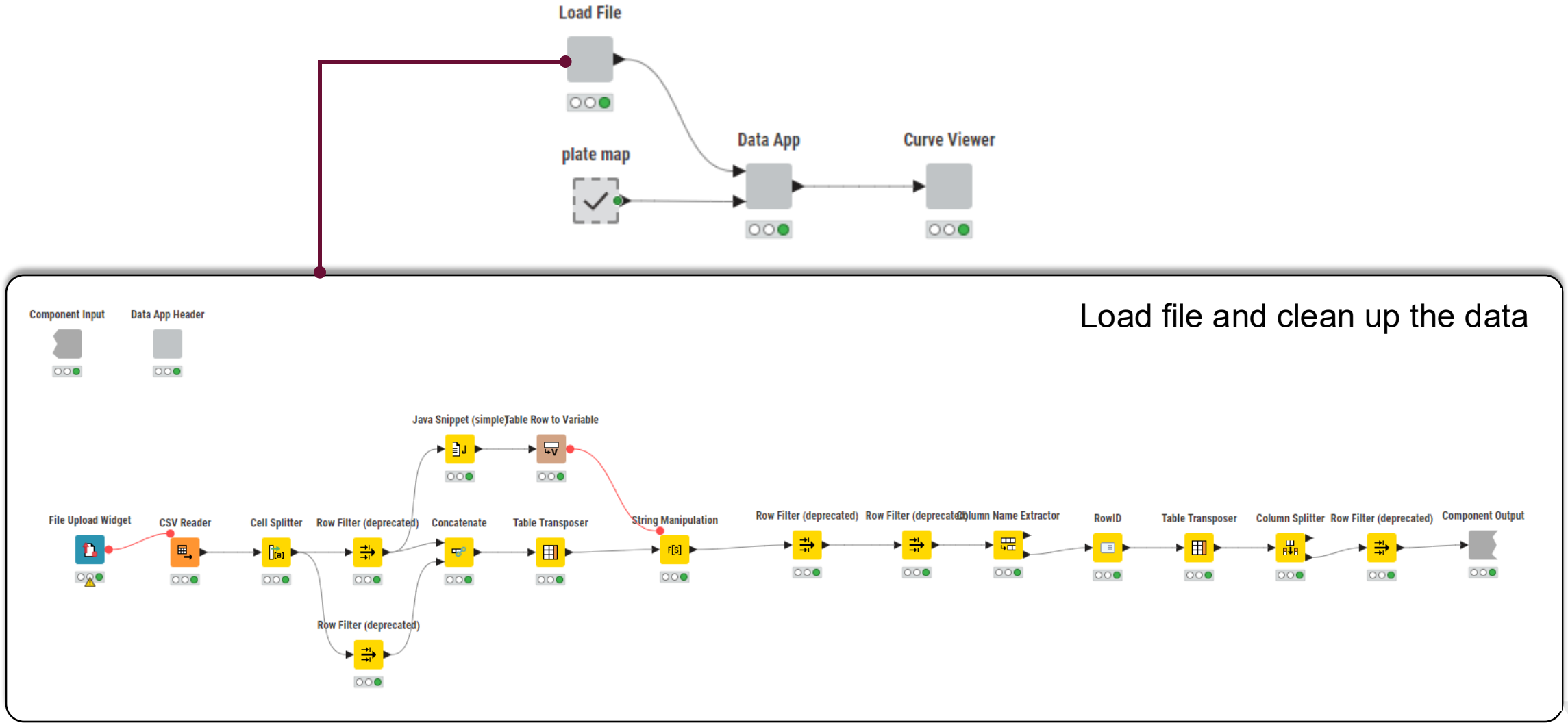
Instrument reads data from 384-well plates and exports .csv files for further analysis – multiple formats are available

	A	B	C	D	E	F	G	H	I	J	K	L
1	Plate information											
2	Plate	Repeat	Barcode	Measured	Chamber t	Chamber t	Humidity a	Humidity a	Ambient te	Ambient te	Group	Label
3	1	1		11.92	30.03	30.08	13.7	13.8	24.17	23.97	1	
4												
5	Background information											
6	Plate	Label	Result	Signal	Flashes/Ti	Meastime	MeasInfo					
7	1		0	83	500	00:00.0						
8												
9	Results - channel 1 (RFU)											
10		1	2	3	4	5	6	7	8	9	10	1
11	A	2467	1340	1667	1675	1879	1572	1720	1629	1817	1574	168
12	B	2384	2600	1681	1778	1648	1699	1727	1776	1642	2136	164
13	C	2435	2133	1754	1752	1771	1620	1710	1863	1758	1747	178
14	D	2244	2493	1766	1813	1717	1767	1662	1846	1826	1791	169
15	E	2306	2522	1872	1878	1837	1702	1947	1738	1739	1817	204
16	F	1558	1903	1700	1795	1707	1855	1740	1760	1817	1714	178
17	G	1781	1843	1779	1764	1798	1791	1848	1720	1755	1682	177
18	H	1729	1802	1704	1826	1821	1832	1774	1810	1823	1850	166
19	I	1801	1731	1985	1941	1909	1871	1882	1810	1924	1788	174
20	J	1678	2455	1841	1822	1819	1922	1749	1818	1821	1797	181
21	K	1682	1786	1907	1888	1854	1769	1807	1856	1773	1730	174
22	L	1536	1850	1763	1843	1830	1762	1788	1777	1803	1792	180
23	M	2151	1767	1842	1751	1879	1712	1944	1750	1790	1709	184
24	N	1665	1789	1865	1791	1809	1867	1835	1773	1738	1795	172
25	O	1710	1694	1805	1732	1797	1725	1785	1758	1680	1648	182
26	P	1487	1611	1667	1699	1666	1650	1591	1685	1648	1626	165
27												

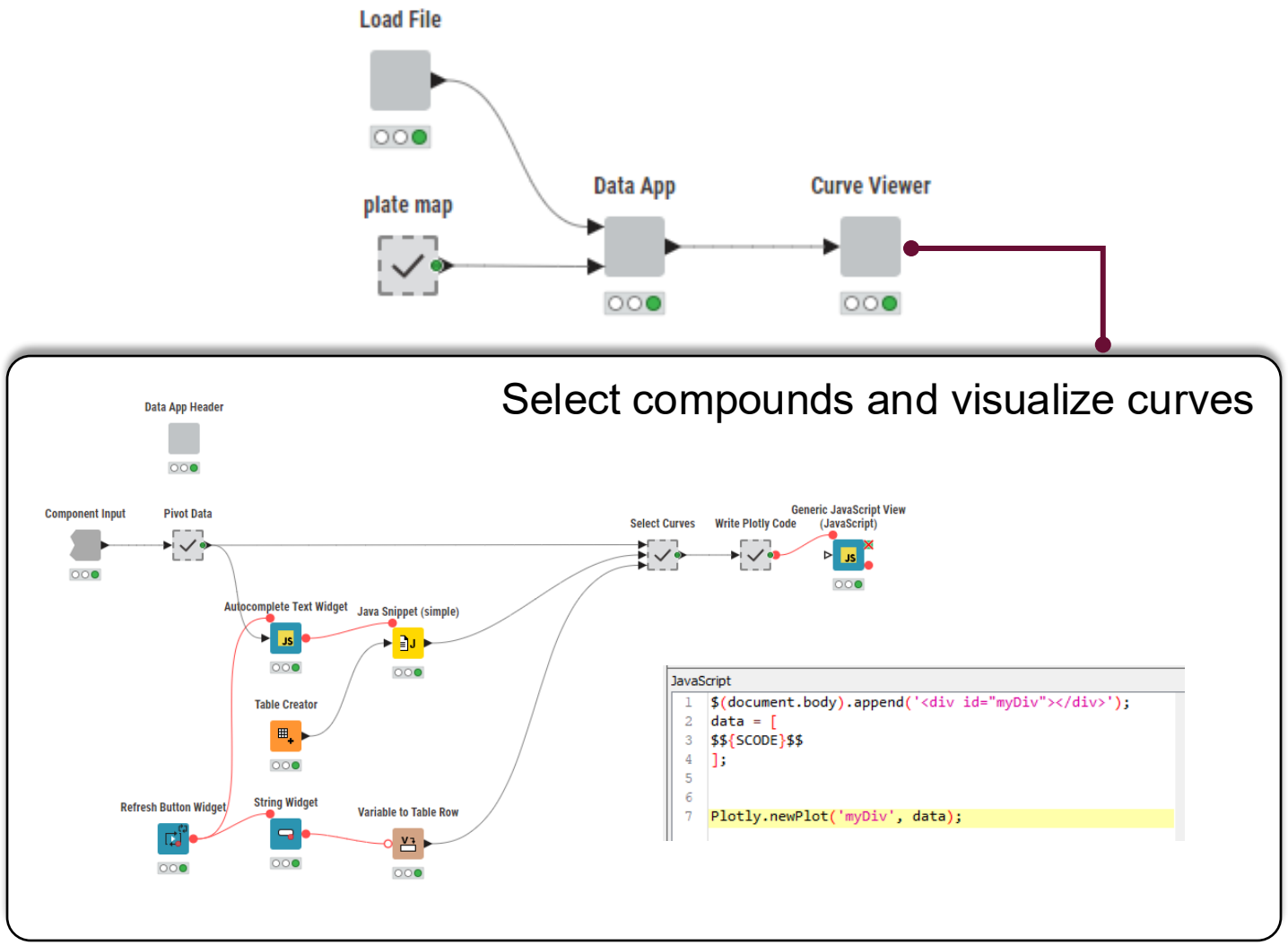
	A	B	E	O
68				
69	PlateNumber	PlateRepeat	Well	Result
70	1	1	A01	1953
71	1	2	A01	1921
72	1	3	A01	1916
73	1	4	A01	1925
74	1	5	A01	1938
75	1	6	A01	1945
76	1	7	A01	1878
77	1	8	A01	1890
78	1	9	A01	1895
79	1	10	A01	1858
80	1	11	A01	1910
81	1	12	A01	1929
82	1	13	A01	1881
83	1	14	A01	1941
84	1	15	A01	1851
85	1	16	A01	1872
86	1	17	A01	1909

Even though data can be exported from the instrument in multiple formats, hours of manual processing and analysis in excel was required

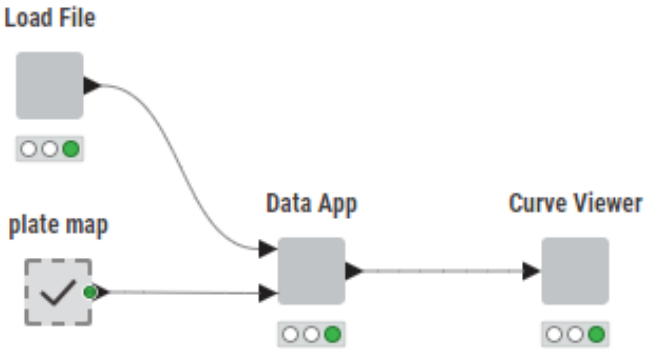
A simple KNIME workflow was developed to load the raw data file and clean it for downstream processing



The ultimate goal is to ensure the data meets quality standards, which is easily facilitated within a data app



Raw data curves can be viewed for quality control using a simple set of data visualizations



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Curve Viewer Tool

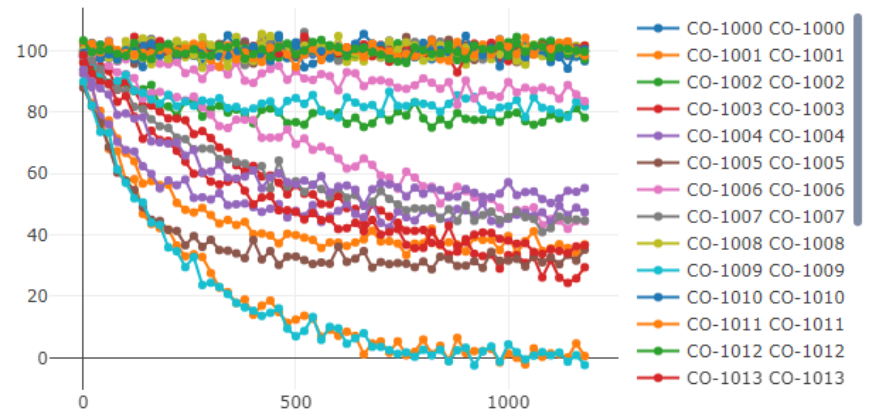
Refresh

Search for Compound

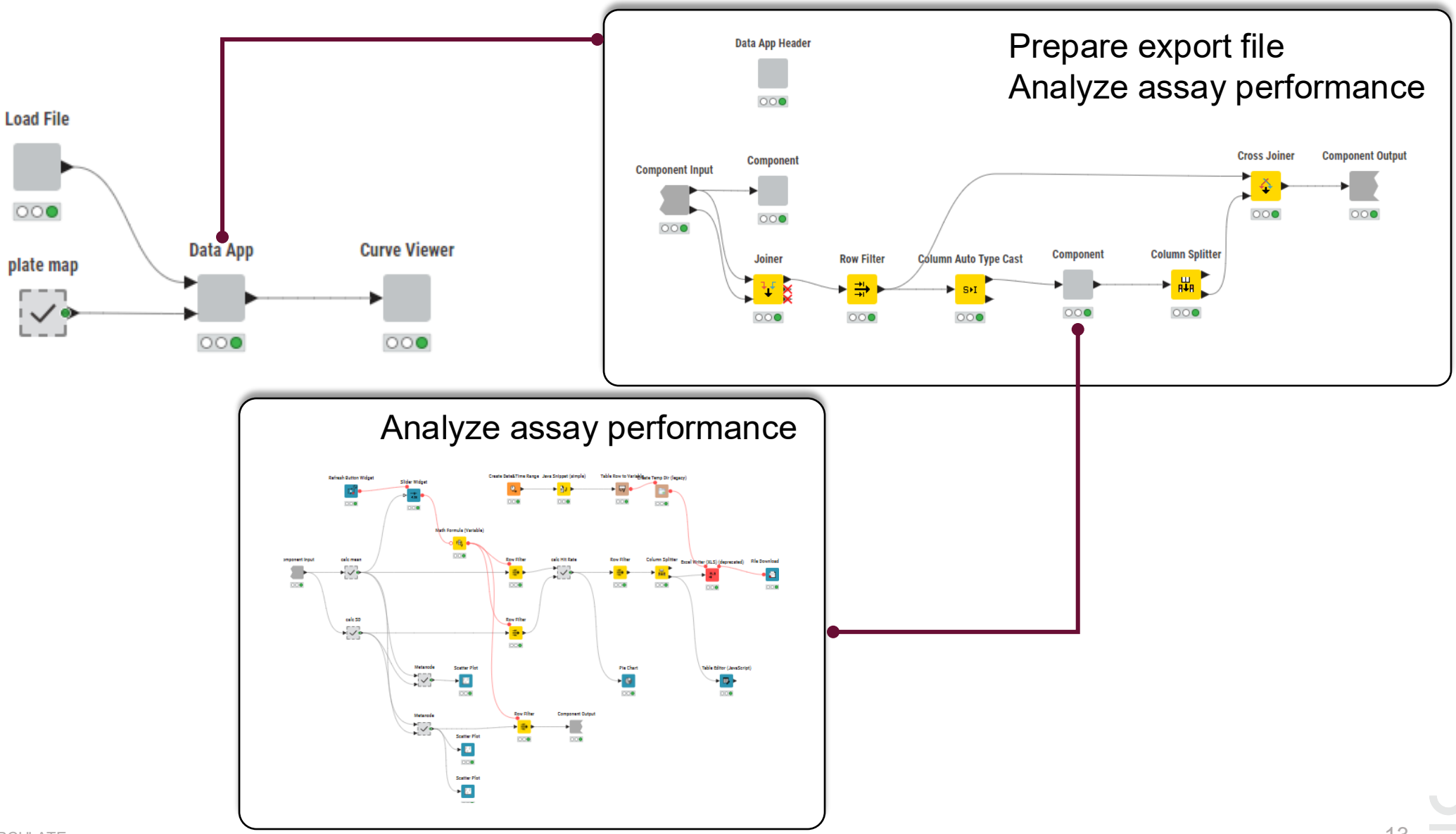
CO-1001

Insert List of Compounds to Display

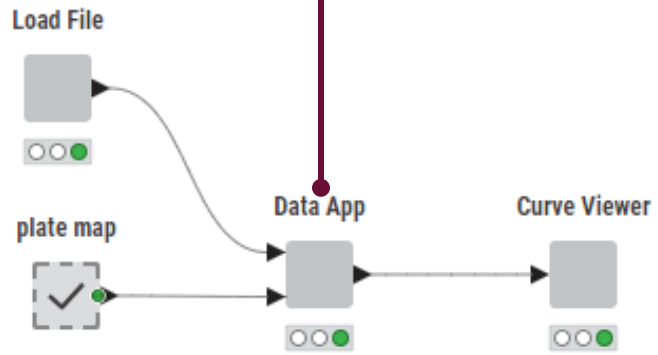
CO-1000
CO-1002
CO-1003
CO-1004
CO-1005
CO-1006
CO-1007
CO-1008
CO-1009
CO-1010
CO-1011
CO-1012

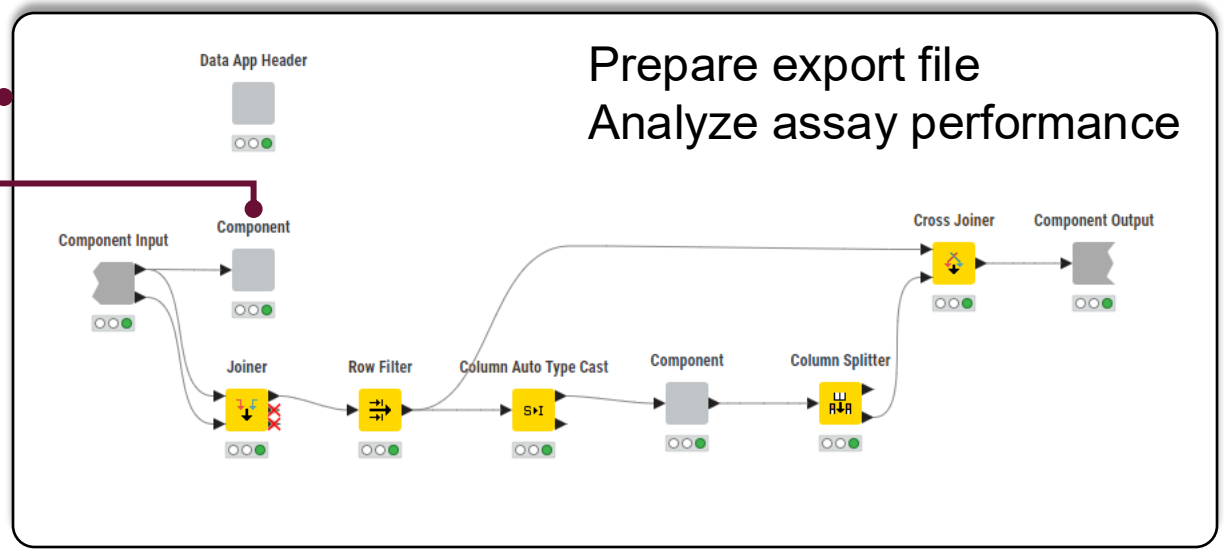


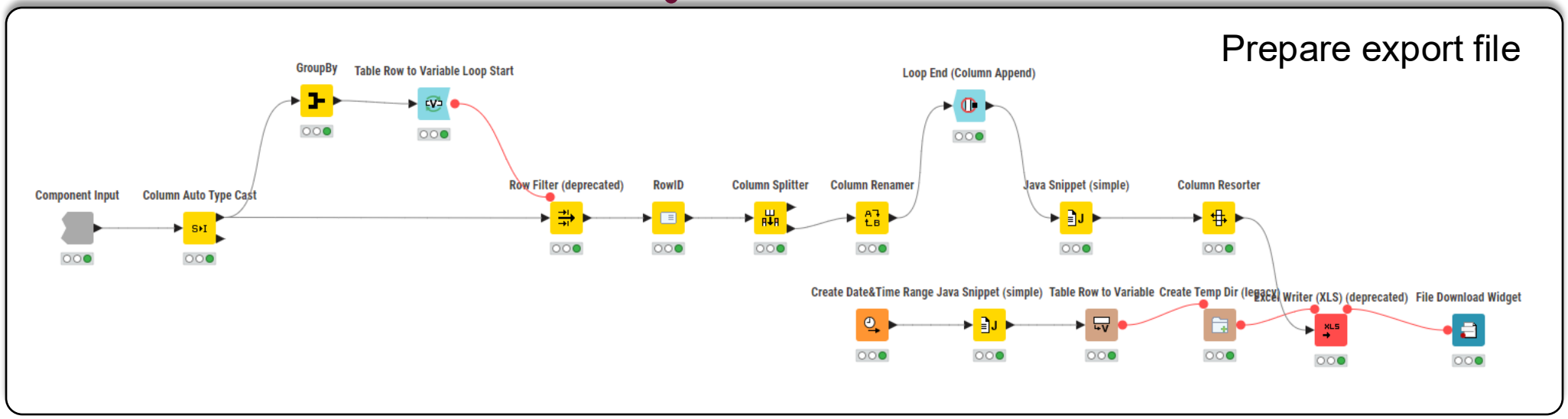
Complex data analysis is accomplished with high fidelity



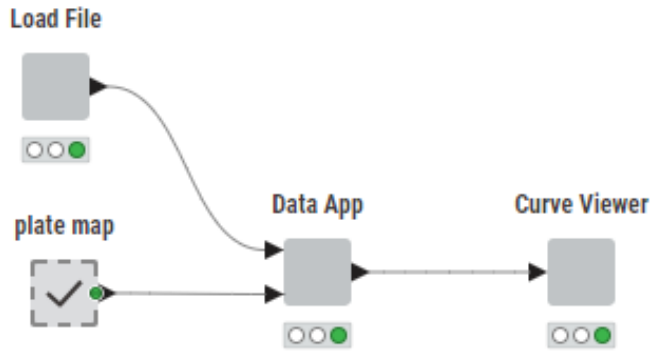
Reconfiguration of data structure for other applications is easily accomplished with KNIME

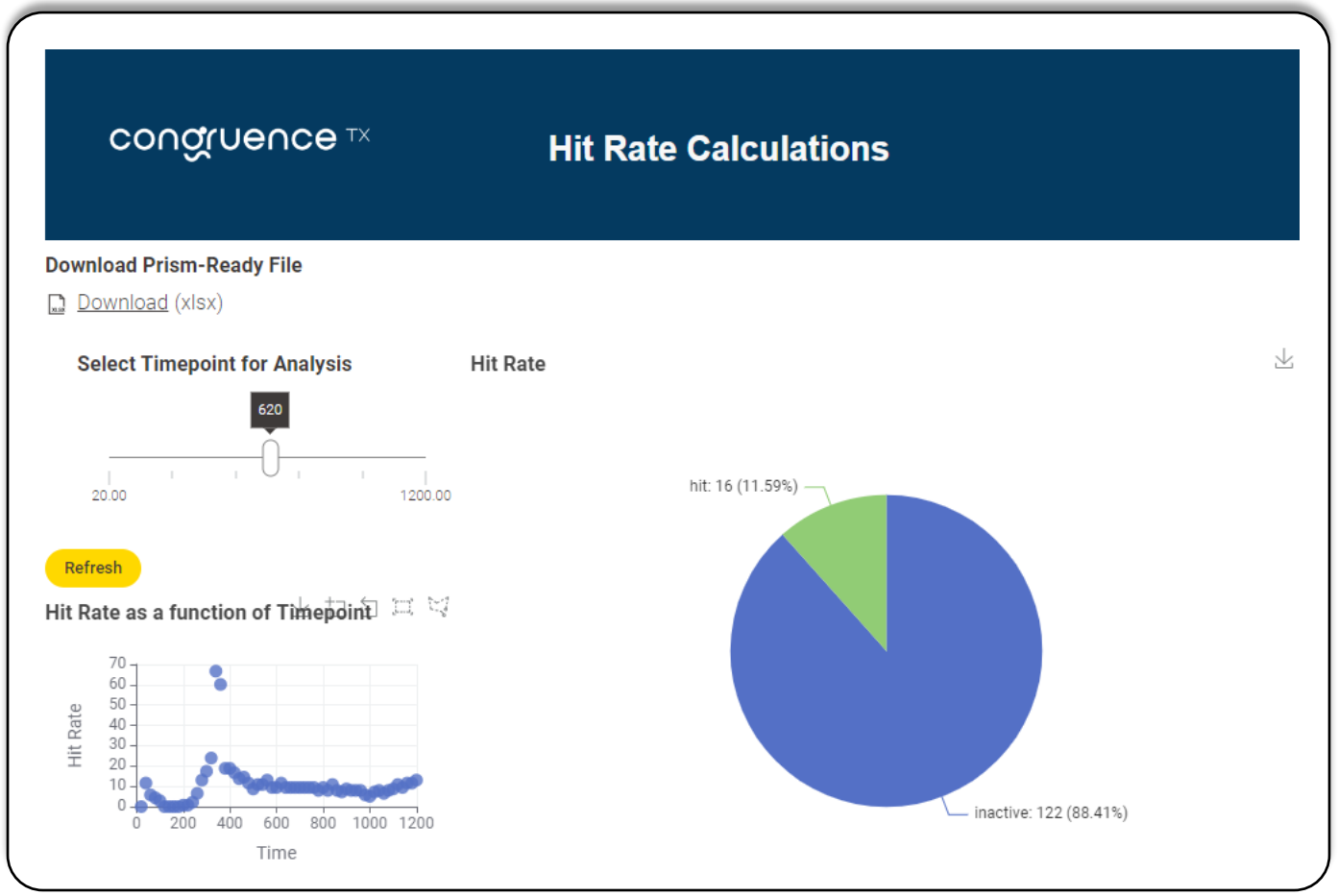






Multiple visualizations within data analysis dashboards allow rapid assessment of experimental success





Automated processing of raw data results in massive time savings for assay scientists

- The KNIME data processing workflow processes the raw data file from our screening assay in seconds, giving back precious time to highly skilled scientist to conduct high value work.
- Task is carried out ~1000x faster with KNIME
- 8-10% time savings per assay, per week, per scientist
- With a lab of 5 scientists, running 2 assays per week, savings is approximately the cost of **one fulltime employee**

Key Takeaways

- In medicinal chemistry, the central paradigm of compound optimization follows a Design-Make-Test-Analyze cycle that is iterated over as efficiently as possible.
- Aggregating predictions, biological data and other cheminformatic outputs enables informed decision making in drug discovery.
- The KNIME Business Hub allows for flexible deployment of workflows, services and data apps that facilitate decision making and accelerate drug discovery.
- Automated processing of raw data results in massive time savings for assay scientists, recovering as much as 20% in time spent analyzing data.
- KNIME evangelism helps maximize the value of data analytics investments by empowering more users to build, share, and scale data solutions efficiently across the organization.