

Introduction of Galaxi – The WuXi AppTec Virtual Space

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GalaXi (WuXi AppTec & BioSolveIT) – The WuXi AppTec Virtual Space



Launched in 2019



GalaXi™

Powered by BioSolveIT

1

50M virtual compounds

- ✓ Building Block docking
- ✓ > 90K Building Blocks
- ✓ > 38 reactions, >128 protocols
- ✓ ~75% success rate, CT 4-6 weeks

More coming soon

3

0.6B virtual compounds

- ✓ >20K drug like core & building blocks
- ✓ More BBs coming soon
- ✓ ~80% success rate, CT 6-8 weeks

More coming soon

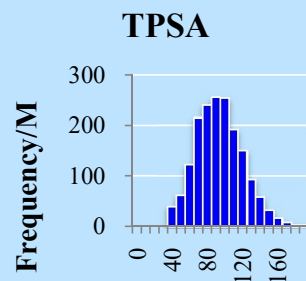
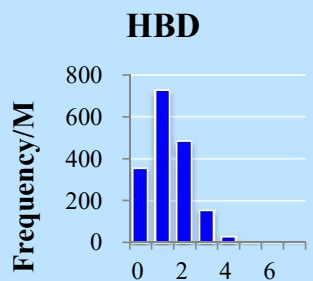
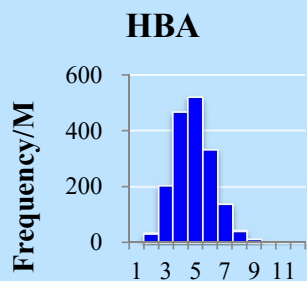
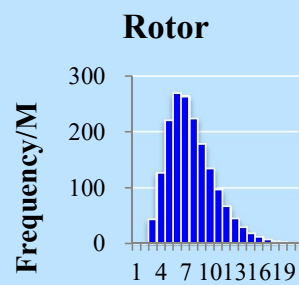
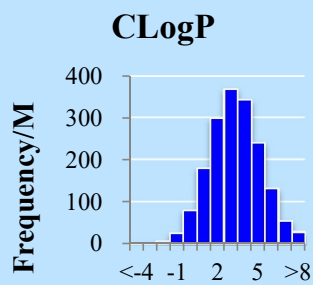
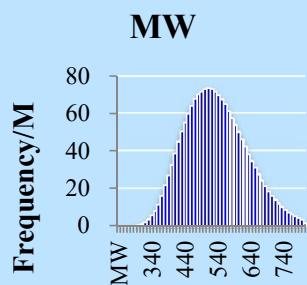
2

1.7 B virtual compounds

- ✓ WuXi unique template
- ✓ WuXi unique BBs
- ✓ More reaction types, more protocols
- ✓ ~80% success rate, CT 6-8 weeks

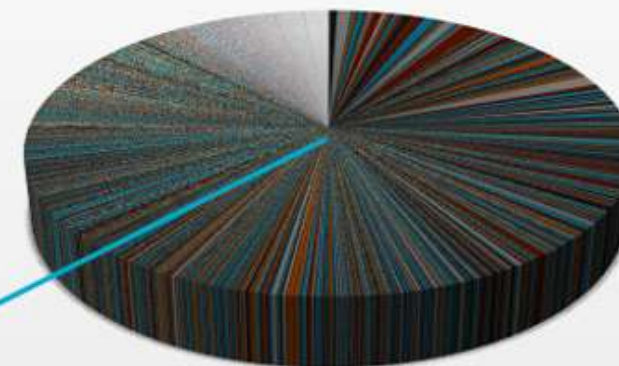
More coming soon

Profiles



Diversity

Cluster Size

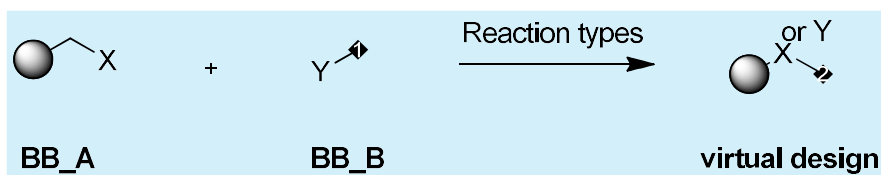


Sample 116,540 compounds

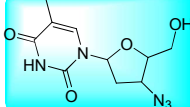
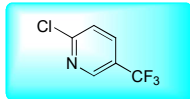
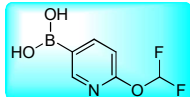
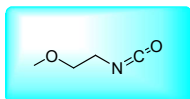
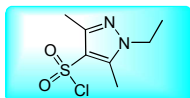
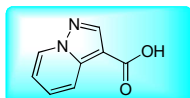
- Bemis-Murcko framework
- Cover **10,353** frameworks
- Size range for each framework: **1 - 1,362**
- Average size for each framework: **11.3**
- Most frequently (>0.2%) occurring **79** frameworks, only account for **24%** of whole DB

Part 1: Building Block Docking

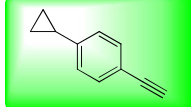
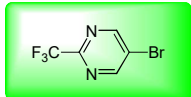
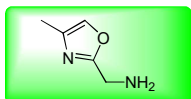
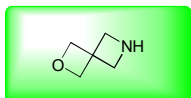
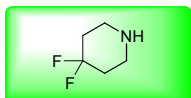
50M Virtual Compounds, novelty, diversity, chemistry feasibility



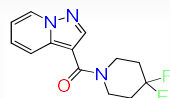
Examples:



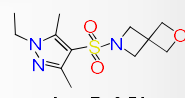
Examples:



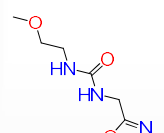
Example Products:



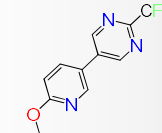
Log P: 1.39
tPSA: 35.91
CLogP: 0.816563



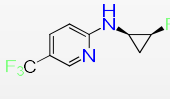
Log P: 0.51
tPSA: 62.21
CLogP: 0.48175



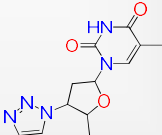
Log P: -0.51
tPSA: 71.95
CLogP: -0.586



Log P: 3.55
tPSA: 46.31
CLogP: 2.37918



Log P: 1.84
tPSA: 24.39
CLogP: 3.03532



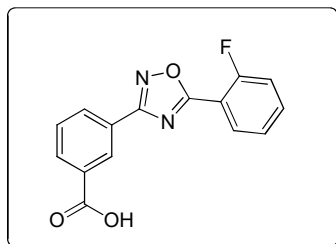
Log P: -0.16
tPSA: 106.83
CLogP: -1.173

- ◆ Acylation
- ◆ Ester formation
- ◆ S-Alkylation
- ◆ Aldol condensation
- ◆ Halogenation reaction
- ◆ Saponification
- ◆ Amide Formation
- ◆ Heck reaction
- ◆ Sonogashira reaction
- ◆ Amine-ester exchange
- ◆ Hydrolysis
- ◆ Stille Coupling
- ◆ Appel Reaction
- ◆ Mitsunobu reaction
- ◆ Strecker Synthesis
- ◆ Buchwald reaction
- ◆ N-Displacement
- ◆ Sulphonamide Formation
- ◆ Carbamate formation
- ◆ Negishi Coupling
- ◆ Suzuki Coupling
- ◆ Chan-Lam Coupling
- ◆ O-Displacement
- ◆ Ugi multicomponent reaction
- ◆ Click Chemistry
- ◆ Oxidation reaction
- ◆ Ullmann reaction
- ◆ Condensation
- ◆ Protection
- ◆ Urea Formation
- ◆ Conjugate addition
- ◆ Reduction
- ◆ Weinreb ketone synthesis
- ◆ De-methylation
- ◆ Reduction Amination
- ◆ Wittig reaction
- ◆ De-protection
- ◆ Ring Formation

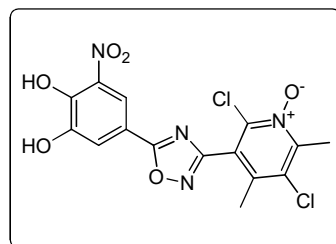
- ◆ 90,610 commercially BBs, including novel WuXi catalogue Building Blocks
- ◆ 38 reaction types, 128 well validated reaction protocols
- ◆ ~ 50 M virtual compounds designed
- ◆ ~ 75% success rate, delivery CT: 4-6 weeks

eg. Oxadiazole Virtual Compounds in WuXi Virtual Space

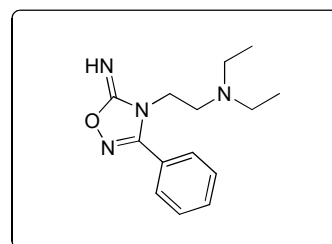
Oxadiazoles are very important cores for drugs or drug candidates



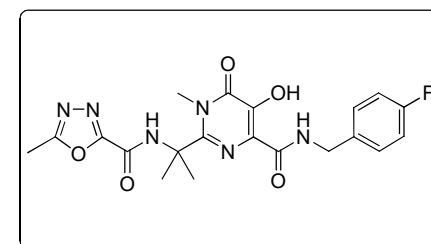
PTC124 for treatment of *Duchenne muscular dystrophy*
Trade name: Translarna
Developed by **PTC Therapeutics**



COMT inhibitor for treatment of *Parkinson's Disease*
Trade name: Opicapone
Developed by **Bial-Portela**

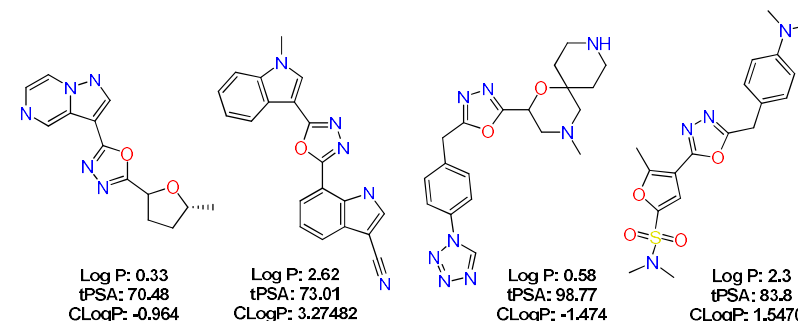
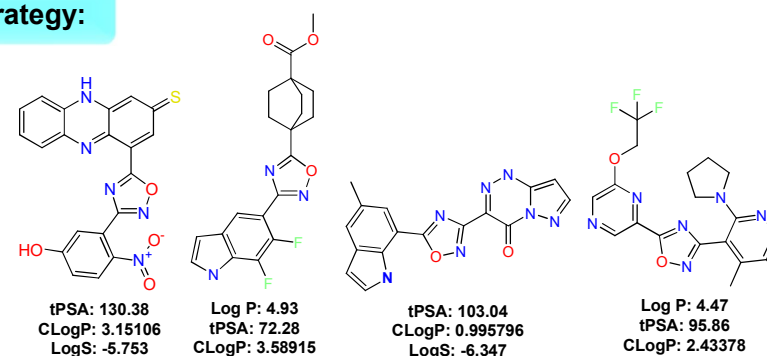
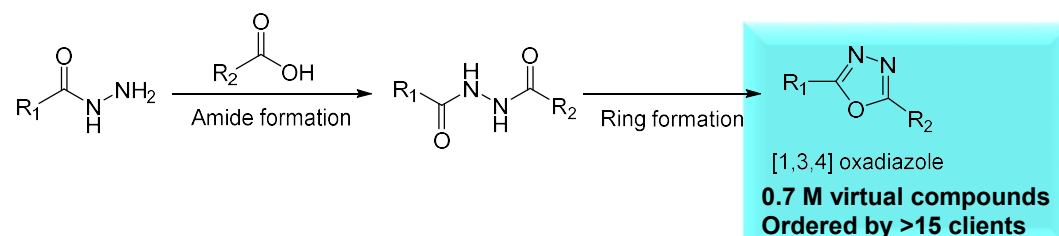
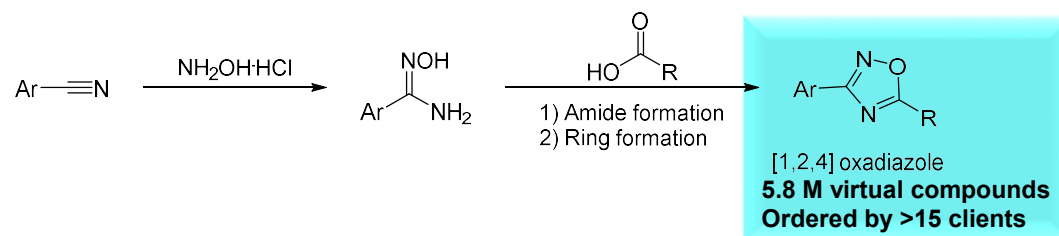


Imolamine for treatment of *angina pectoris*
Trade name: Angolon



Raltegravir for treatment of *HIV infection*
Trade name: Isentress
Developed by **Merck & Co.**

WuXi designed virtual library compounds of oxadiazoles based on below parallel strategy:

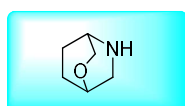
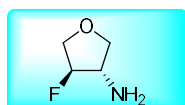
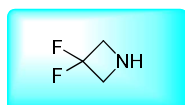
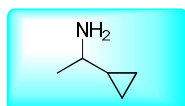
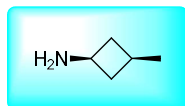
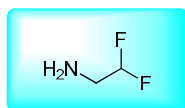


Part 2: WuXi Templates Based Virtual Library

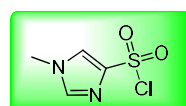
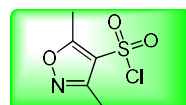
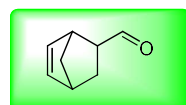
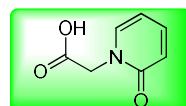
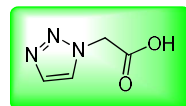
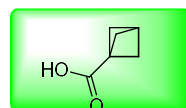
WuXi template based virtual library



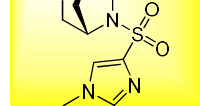
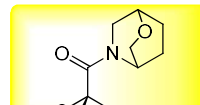
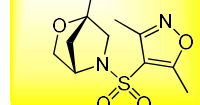
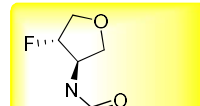
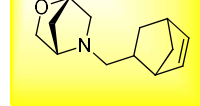
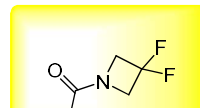
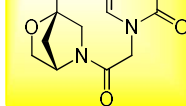
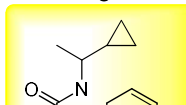
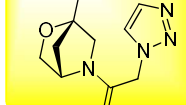
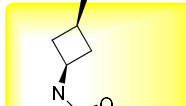
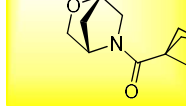
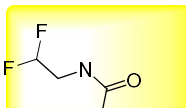
Examples:



Examples:



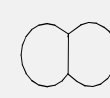
Examples:



Diverse chemo-type



Spiro aliphatic ring
SP



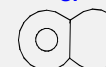
Fused bicyclic aliphatic ring
BC



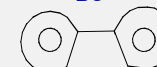
Bridged aliphatic ring
BR



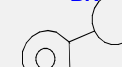
Fused aromatic ring
FAR



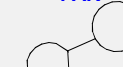
Fused aromatic-aliphatic ring
FAA



Bicyclic aromatic ring
BAR

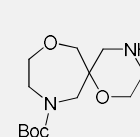


Bicyclic aromatic-aliphatic ring
BAA

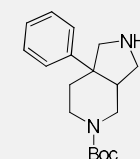


Bicyclic aliphatic ring
BAL

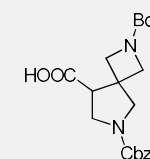
Example for template



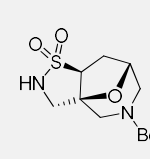
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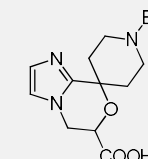
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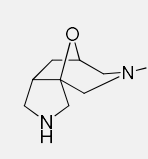
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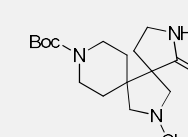
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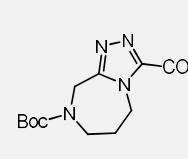
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WX125036



WX105147



WX140047

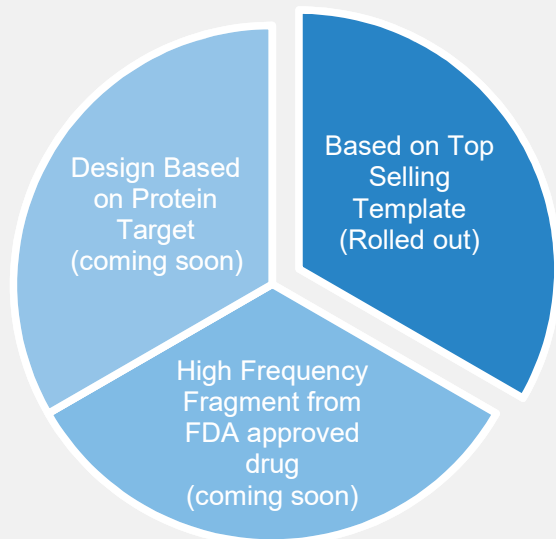
- ◆ ~1.7 B of virtual design prepared.
- ◆ WuXi has 1,000+ templates can be used for future virtual library enumeration.

Part 3: Drug-like Core Based Virtual Library

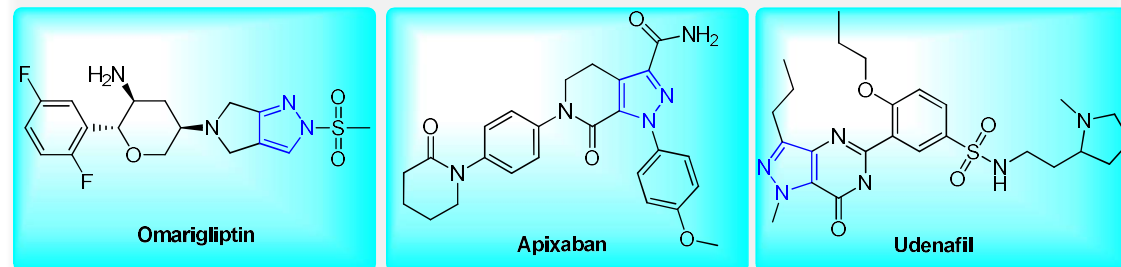
Based on Top Selling Templates (Rolled out)

Drug like cores + R1 $\xrightarrow{1-2\text{steps}}$ KIs $\xrightarrow{19\text{ reaction types}}$ Virtual Library

Drug-like Cores

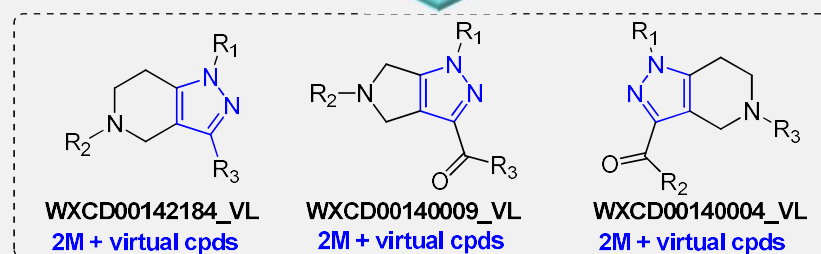
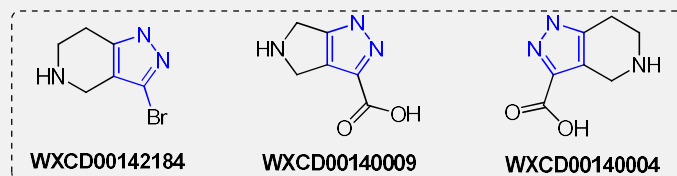


- ◆ 0.6 B virtual compounds designed based on Top Selling templates.
- ◆ The other 2 parts coming soon.



Pyrazole played very important role for drugs or drug candidates, showed above.

WuXi has well sold templates:



WuXi Virtual Library Summary

Accessible Ways

1

SMILES in csv

- ~50 M for phase 1
- ~1.7 B for phase 2
- ~0.6 B for phase 3
- SMILES for virtual library

<https://www.labnetwork.com.cn/frontend-app/p/#!/library/virtual>

- Csv file size, >400 GB
- ~12 GB compressed as 7z file

2

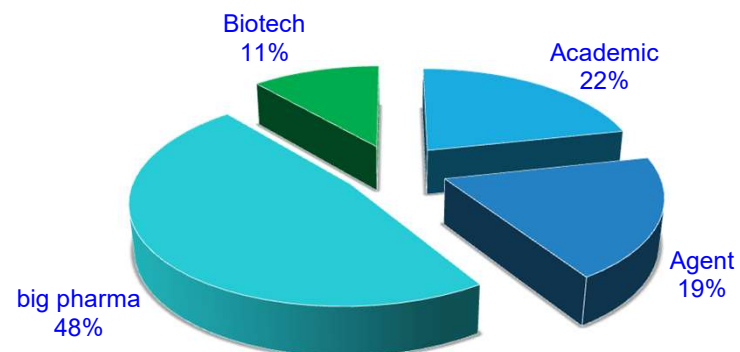
GalaXi

- Collaborate with BioSolveIT
- Fragment base
- ~50 M for phase 1
- ~1.7 B for phase 2
- ~0.6 B for phase 3

https://www.biosolveit.de/in/finiSee/#chemical_spaces

- File size ~60 MB
- Similarity searching in 1 min

Customer Distribution



- More than 100 orders in the past 2 years.
- Delivered thousands of final compounds.

Instruction for GalaXi – The WuXi Virtual Space

Searching

5. Save

3. Starting search

2. Setting

1. Paste structure

4. Result showing here

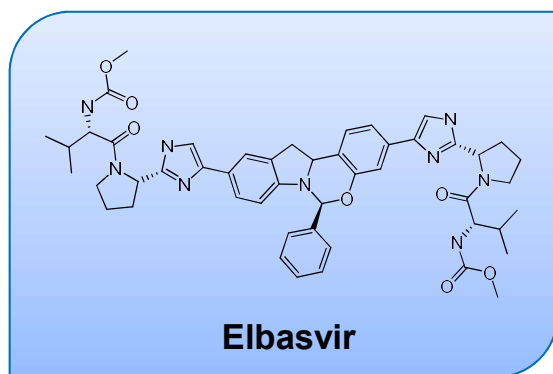
The screenshot shows the inSight software interface. On the left, a menu is open with options: Clear Local Host (Ctrl+N), Load Molecule... (Ctrl+O), Save Solutions As... (Ctrl+S), and About inSight. A 'total Diversity' slider is set to 1.00. The central workspace displays the chemical structure of Zanutrutinib, labeled 'Zanutrutinib BTK Inhibitor'. Below the structure, the text 'Matching' is visible. On the right, a 'Results' table is shown with columns for 'Molecule', 'Similarity', 'Source', and 'Name'. The table contains four rows of results, each with a checked checkbox in the first column.

	Molecule	Similarity	Source	Name
<input checked="" type="checkbox"/>		0.915	2.1bn-GalaXi_2020-11	WXVL017__SB2092__NT0403
<input checked="" type="checkbox"/>		0.915	2.1bn-GalaXi_2020-11	WXVL017__SB2092__NT0066
<input checked="" type="checkbox"/>		0.915	2.1bn-GalaXi_2020-11	WXVL017__SB2092__NT0376
<input checked="" type="checkbox"/>		0.911	2.1bn-GalaXi_2020-11	WXVL018__SB2092__J0152

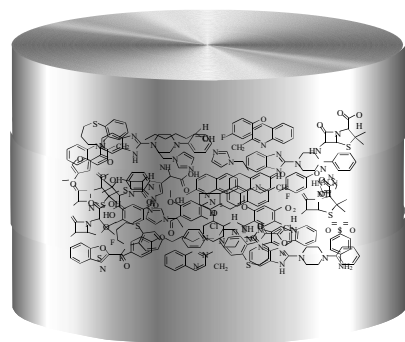
https://www.biosolveit.de/inSight/#chemical_spaces

Illustration for GalaXi – The WuXi Virtual Space

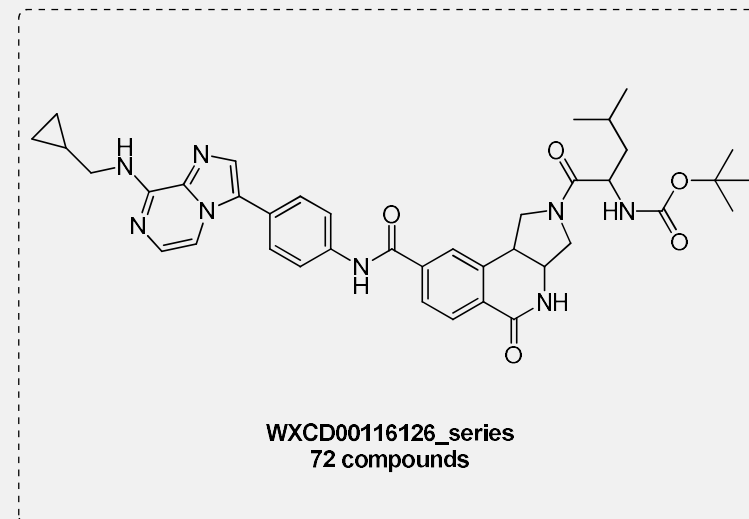
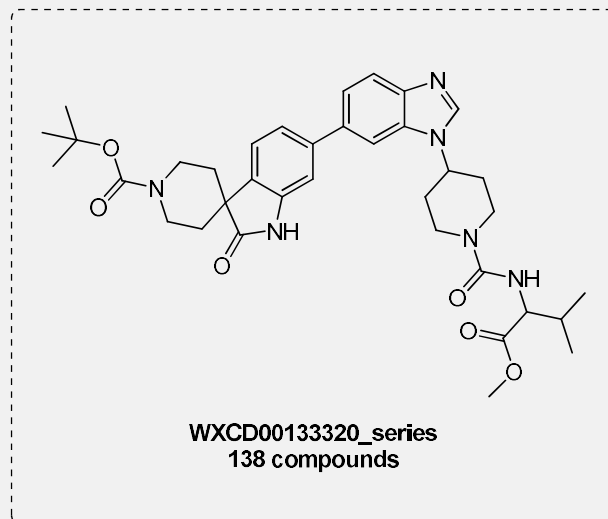
Searching result



New Chemo types found,
Top 1,000 similar compounds

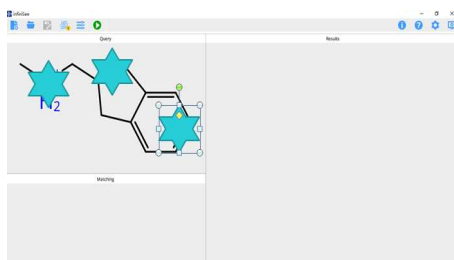


GalaXi™
Powered by 



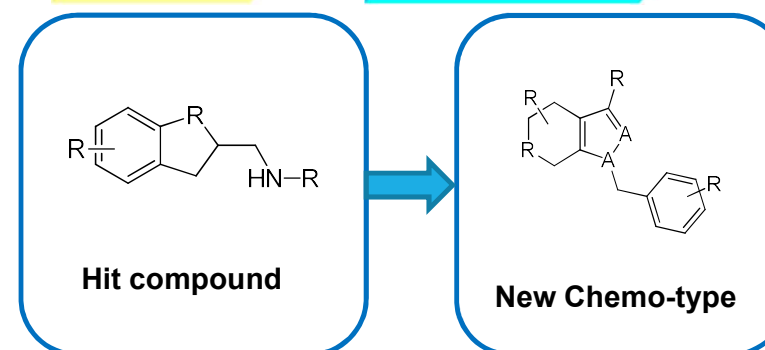
GalaXi – The WuXi Virtual Space Support Hit Finding

Case 1



# of ID	Compound ID	Similarity
1	WXVL_compound 1	0.98
2	WXVL_compound2	0.98
	
2,000	WXVL_compound2000	0.80

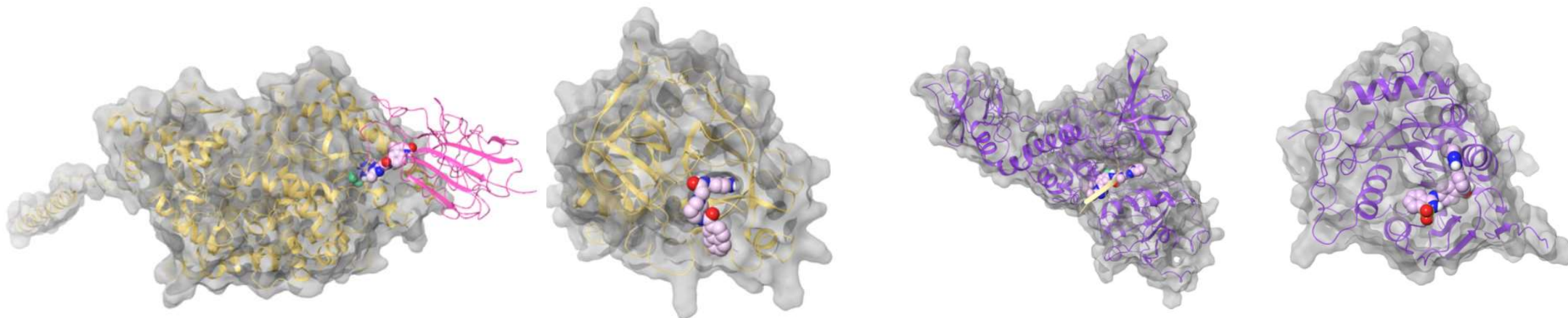
Rank	MolfileName	Binding Energy
1	WXVL_compound1	-9.5
2	WXVL_compound2	-9.4
3	WXVL_compound3	-9.4
4	WXVL_compound4	-9.4
5	WXVL_compound5	-9.4
6	WXVL_compound6	-9.4
7	WXVL_compound7	-9.4
8	WXVL_compound8	-9.4
9	WXVL_compound9	-9.0
10	WXVL_compound10	-9.0



- ◆ Compound 2 and other 7 compounds were new Chemo-Type.
- ◆ Compound 4&7 were more active based on Bio Assay result.
- ◆ A follow-up library with 100 compounds was designed with the new chemo-type and more active compounds were found.

The WuXi Virtual Space - Hits Finding for COVID19

Case 2



17 critical SARS-CoV-2 proteins, 40 different target sites <https://vf4covid19.hms.harvard.edu/>

Monomer Supply Support to Virtual Compounds

Reagent Acquisition



WuXi Stock

Lead time: 0-1 working day

Building Block Classification	# of reagents
Carboxylic Acid/ Acid Chloride	5,962
Amine	6,133
Boronic Acid/Ester	1,318
Alcohol	2,548
Aryl/Heteroaryl Halide	4,479
Aldehyde/Ketone	1,951
Sulphonyl Chloride / Isocyanate	348
WuXi Template/Scaffold	14,476
Total	37,215



Lead time: 3-4 working days

Building Block Classification	# of reagents
Carboxylic Acid/ Acid Chloride	37,126
Amine	62,093
Boronic Acid/Ester	6,635
Alcohol	35,661
Aryl/Heteroaryl Halide	65,311
Aldehyde/Ketone	7,762
Sulphonyl Chloride / Isocyanate	1,712
Alkyne/hydrazine	2,952
Total	219,252

WuXi Chemistry Platform

02 Hit to Lead

04 Pre-Clinic

06 Commercial

Discovery

Early Development

Full Development

01 Target to Hit

03 Lead Optimization

05 Clinical I - III

CSU

STA

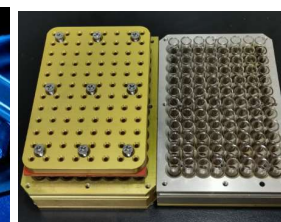
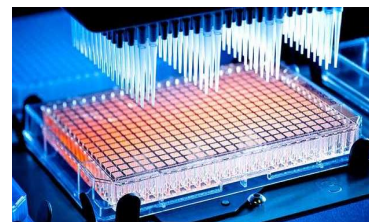
Library Platform

Since 2001

Virtual Library

Library Enrichment

Parallel Medicinal
Chemistry



Thank you very much for your attention!

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