The background of the slide is a complex molecular network. It consists of numerous light blue circles of varying sizes connected by thin grey lines, creating a web-like structure. Overlaid on this network is a silhouette of a human figure. The interior of the silhouette is filled with a dense and colorful array of chemical structures, including rings, chains, and various functional groups in shades of red, yellow, green, blue, and purple. Some structures are more prominent than others, such as a large red circle in the chest area and a blue hexagonal ring in the upper torso.

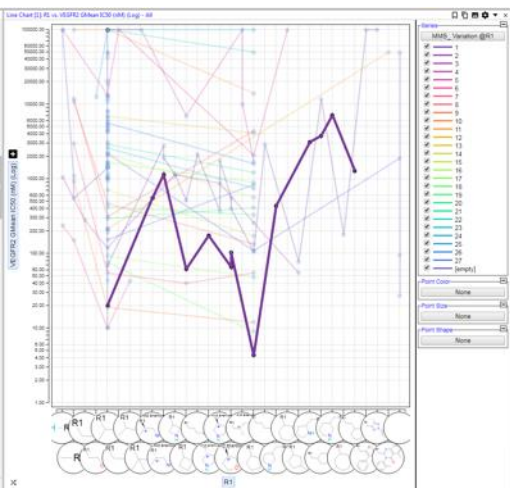
## **Beyond the SARs - Adding More Pizzazz to your Analysis**

**UGM 2019**

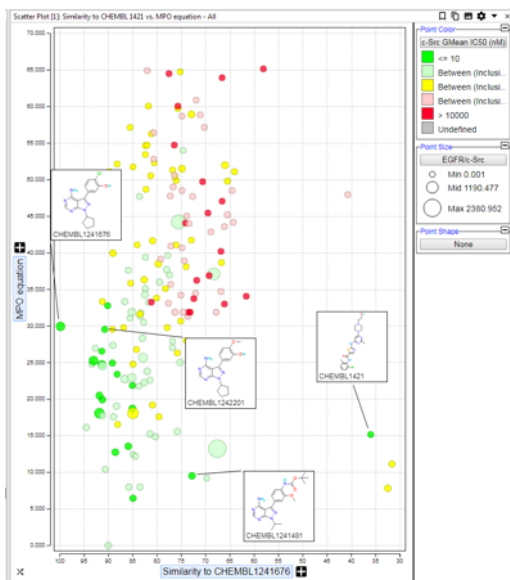
**Dennis Powell  
Senior Consultant**

# Beyond the SARs - Adding More Pizzazz to your Analysis

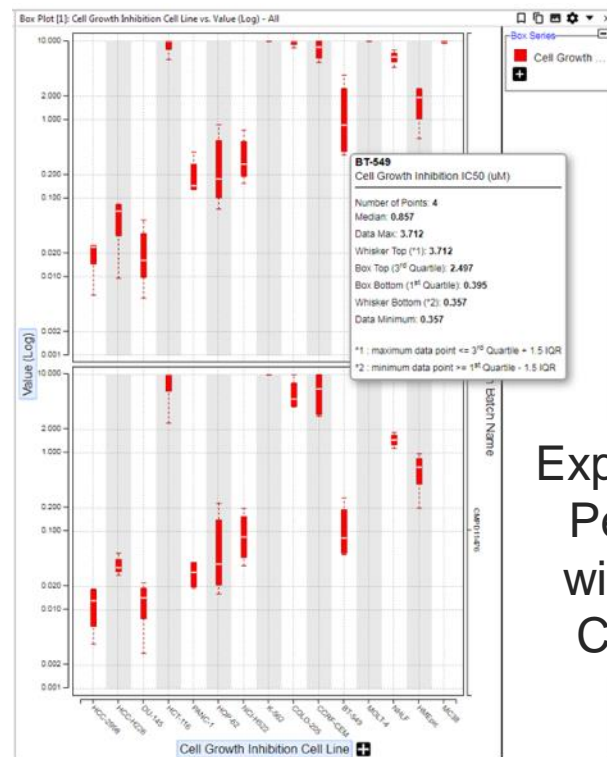
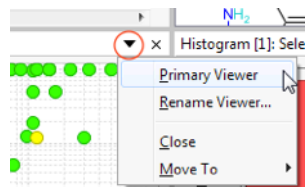
## Exploring Activity Trends in Matched Molecular Series



## Structure Similarity and MPO Scoring- Looking for Interesting Outliers



## Revisiting Favorite Tools

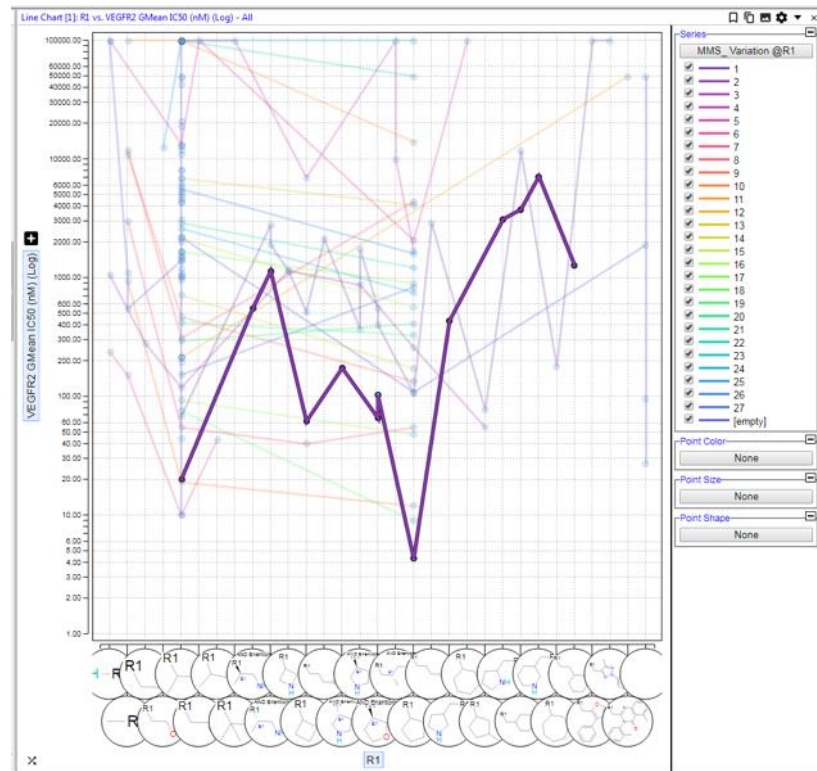


## Exploring Assay Performance with Selected Compounds

|                        |                                |    |      |        |
|------------------------|--------------------------------|----|------|--------|
| Export to Data File... | Cross Target Summary           | 30 | 4.50 | 525.00 |
| Export to Application  | Personal                       |    |      |        |
| Follow-on Query        | 10 Demos                       |    |      |        |
| Edit Cells             | Oncology Project               |    |      |        |
| Append Value           |                                |    |      |        |
|                        | BPS form                       |    |      |        |
|                        | Kinase Project Rgroup Full new |    |      |        |
|                        | Kinase Project Rgroup SP       |    |      |        |
|                        | Kinase Project Rgroup SP pIC50 |    |      |        |

# Exploring Activity Trends in Matched Molecular Series

- There are multiple D360 tools that enable the exploration of Structure Activity Relationships:
  - Chemical Series
  - Structure Similarity Maps
  - R-Group Analysis-RGM
  - Structure Comparison Viewer
  - Matched Molecular Series
- A combination of several of these tools will allow us to graphically examine the change in activity with variations in a specific portion of the structure



# Exploring Activity Trends in Matched Molecular Series-Setup ...

Spreadsheet

|    | CHEMBL Id      | Structure | c-Src GMean IC50 (nM) | EGFR GMean IC50 (nM) | VEGFR2 GMean IC50 (nM) | c-Abl GMean IC50 (nM) | HCK GMean IC50 (nM) | PI3Kalpha GMean IC50 (nM) |
|----|----------------|-----------|-----------------------|----------------------|------------------------|-----------------------|---------------------|---------------------------|
| 1: | CHEMBL1 241676 |           |                       |                      |                        |                       |                     |                           |
| 2: | CHEMBL1 242568 |           |                       |                      |                        |                       |                     |                           |
| 3: | CHEMBL1 241481 |           |                       |                      |                        |                       |                     |                           |
| 4: | CHEMBL1 242656 |           |                       |                      |                        |                       |                     |                           |

- Do an R-Group Analysis

Matched Molecular Series (R-Group) Setup

Select R-Group Columns to include in the analysis:

All Dataset R-Group Columns:

R-Group Columns to Analyze:

CORE  
R1  
R2

Add >  
Add All >>

- Do a Match Molecular Series Analysis

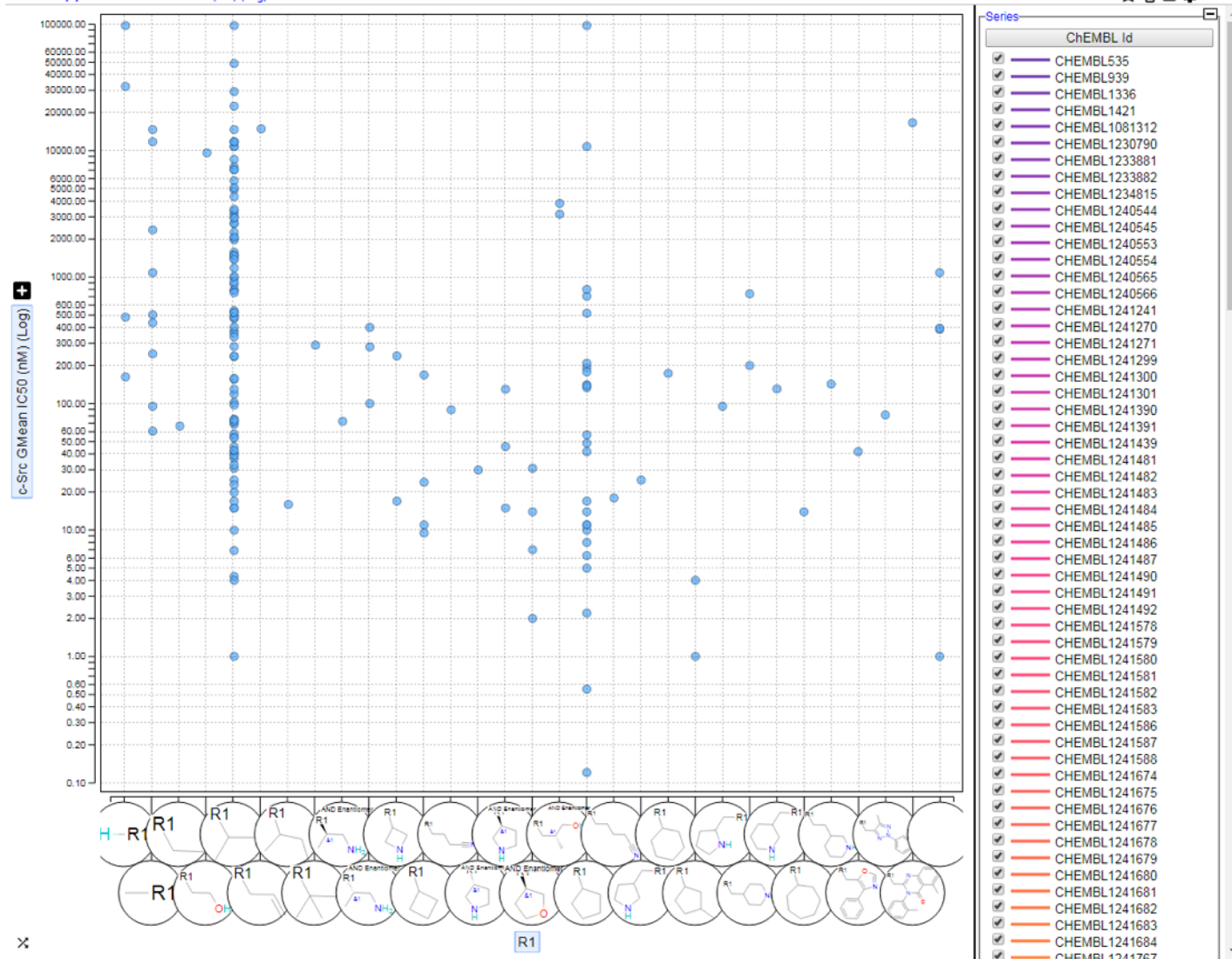
Spreadsheet

|    | CHEMBL Id      | Structure | c-Src GMean IC50 (nM) | EGFR GMean IC50 (nM) | VEGFR2 GMean IC50 (nM) | CORE | R1 | R2 | MMS_Variation @CORE | MMS_Variation @R1 | MMS_Variation @R2 |
|----|----------------|-----------|-----------------------|----------------------|------------------------|------|----|----|---------------------|-------------------|-------------------|
| 1: | CHEMBL1 241676 |           | 0.12                  | 67.00                | 4.30                   |      |    |    |                     | 2                 | 2                 |
| 2: | CHEMBL1 242568 |           | 0.55                  | 318.00               | 106.00                 |      |    |    |                     | 1                 | 2                 |
|    |                |           |                       |                      |                        |      |    |    |                     |                   |                   |

4

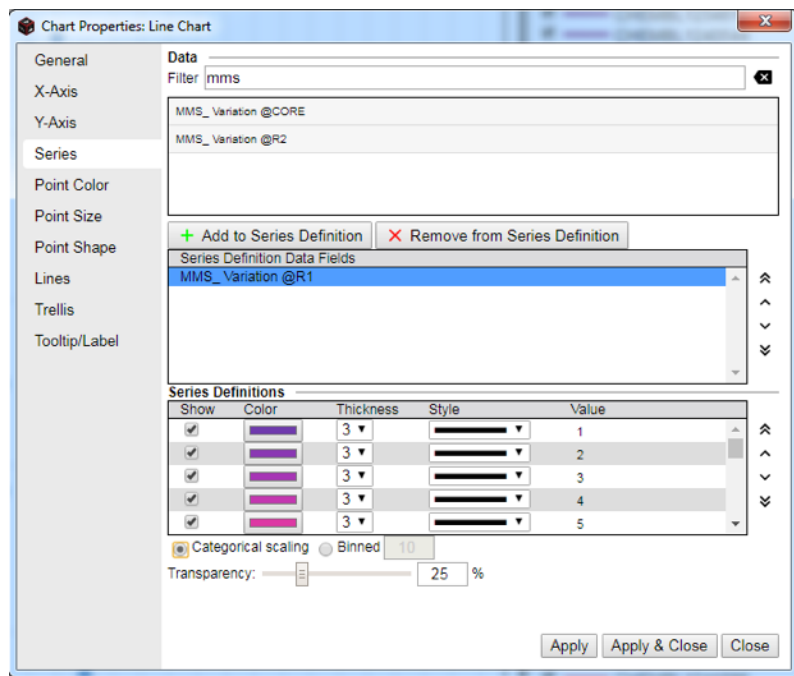
# Exploring Activity Trends in Matched Molecular Series-Line Chart

Line Chart [1]: R1 vs. c-Src GMean IC50 (nM) (Log) - All



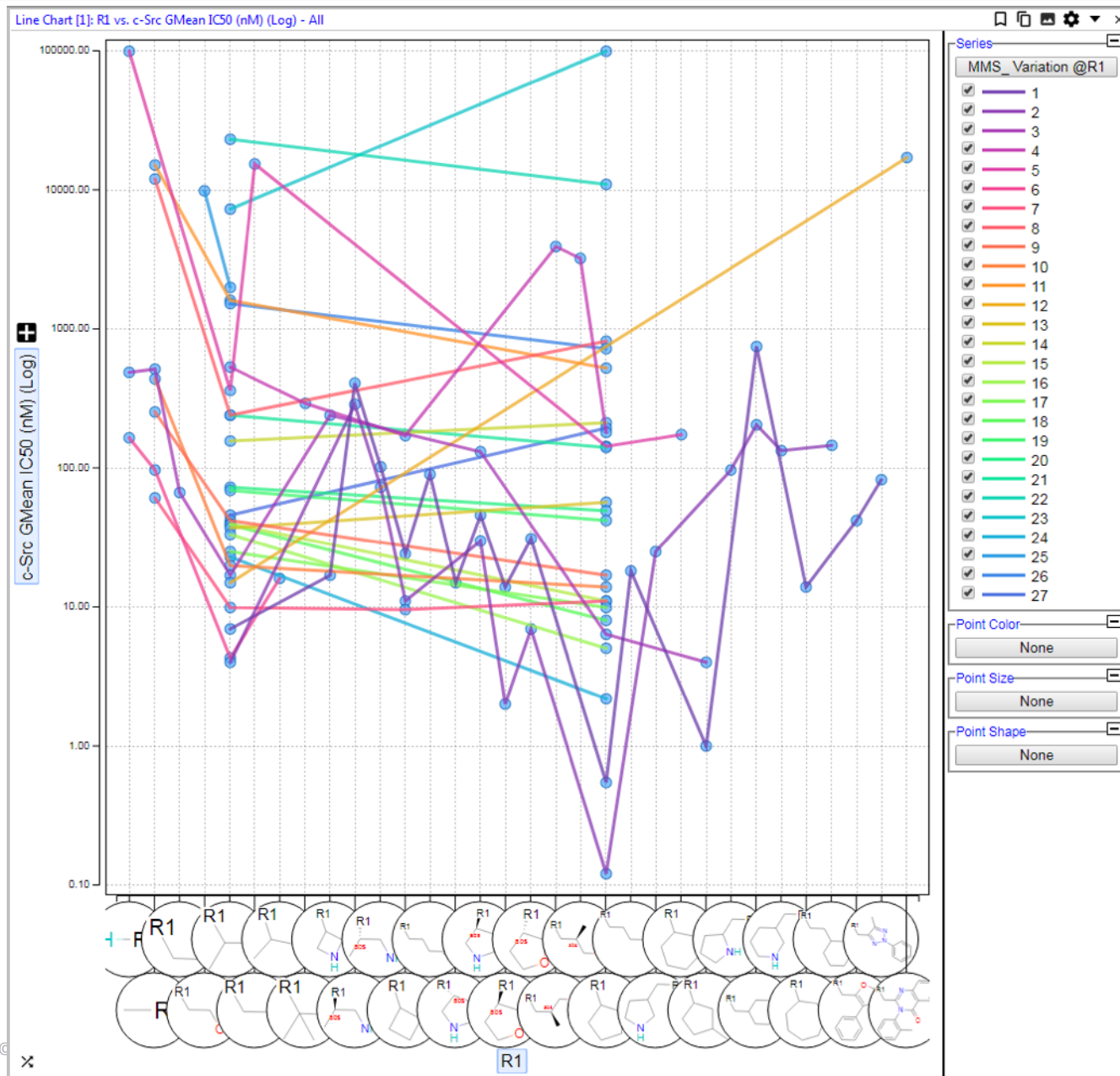
- Create a Line Chart
- Set the X-Axis to R1
- Set the Y-Axis to Desired Property and Log Scaled

# Exploring Activity Trends in Matched Molecular Series-Setting up the Series



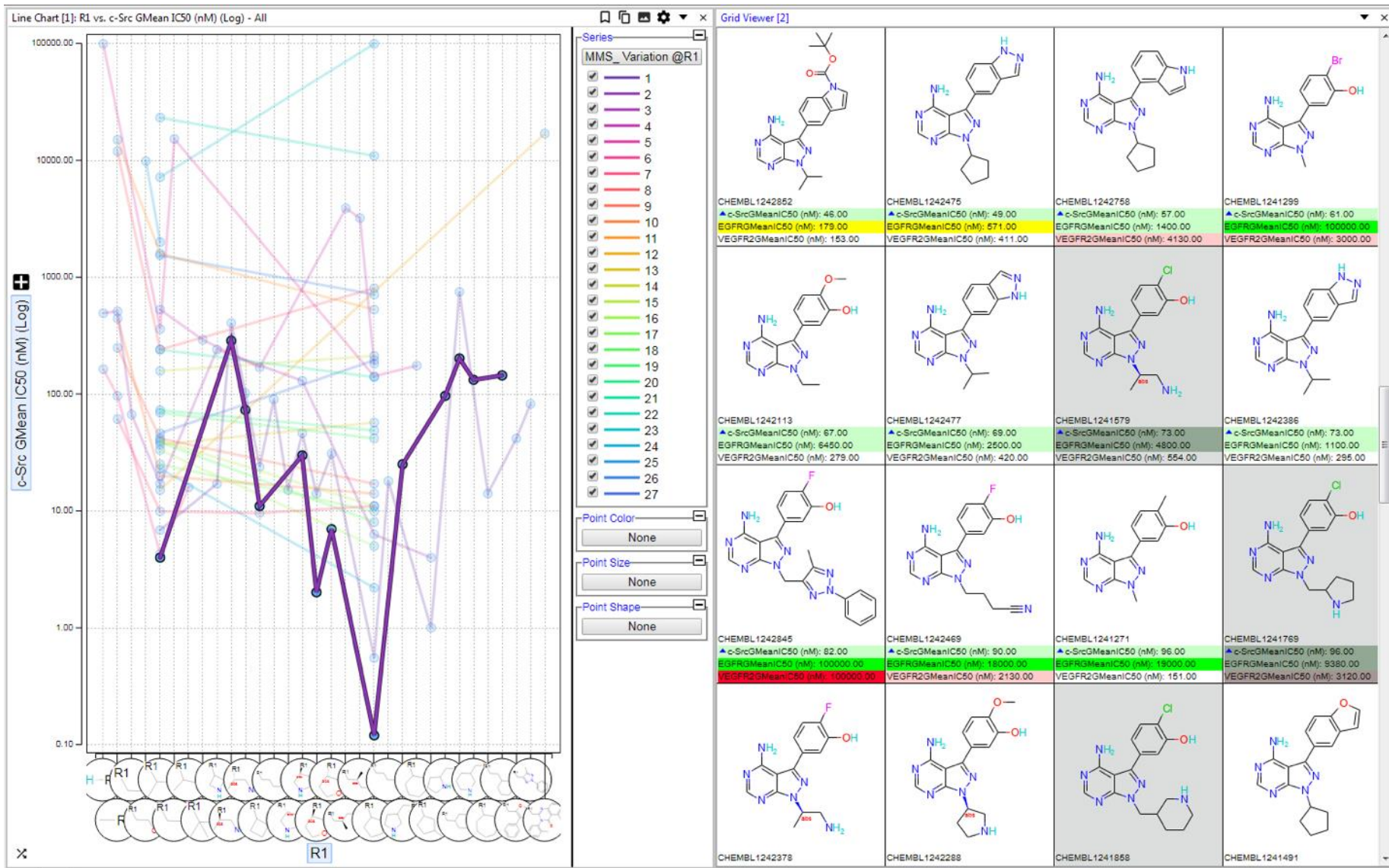
- **Set up the Series to match the X-Axis R-Group**
- **Make the Axis Categorical**

# Exploring Activity Trends in Matched Molecular Series-Connected Line Chart



- Select a line or a Series

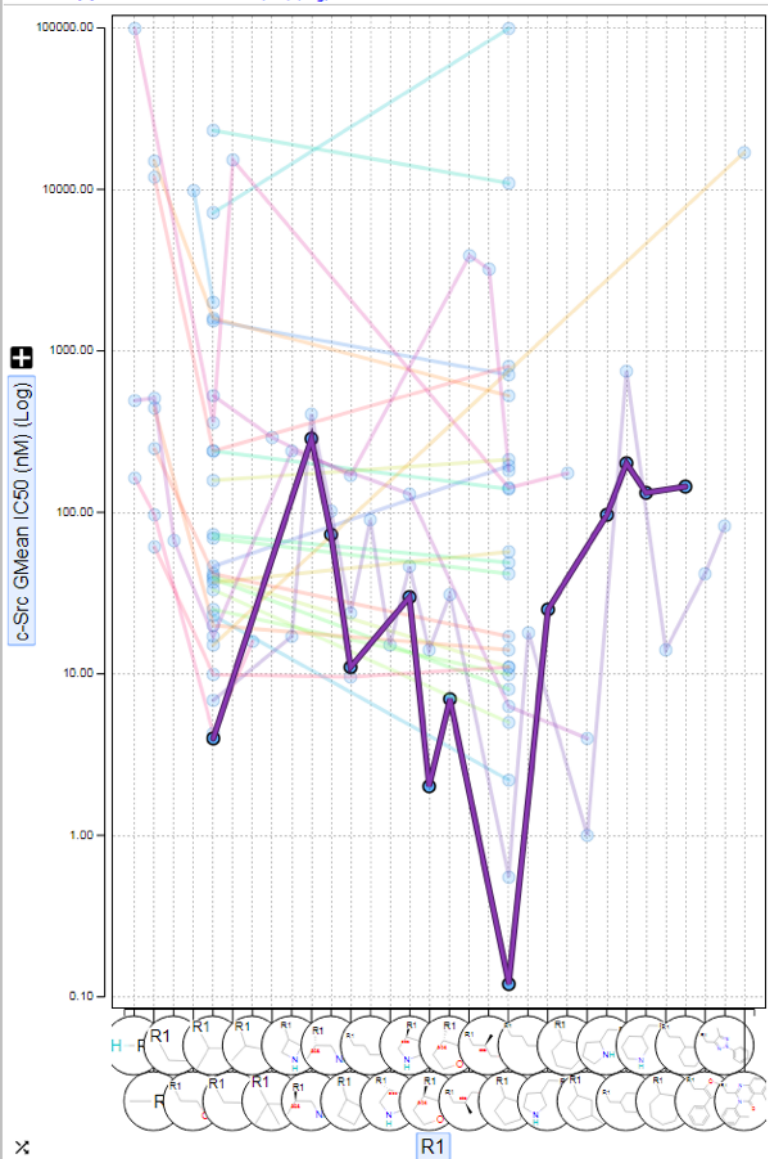
# Exploring Activity Trends in Matched Molecular Series-Add a Grid Viewer





# Exploring Activity Trends in Matched Molecular Series-Primary Viewer mode

Line Chart [1]: R1 vs. c-Src GMean IC50 (nM) (Log) - All



Grid Viewer [2]

**Series**

MMS\_Variation @R1

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25
- 26
- 27

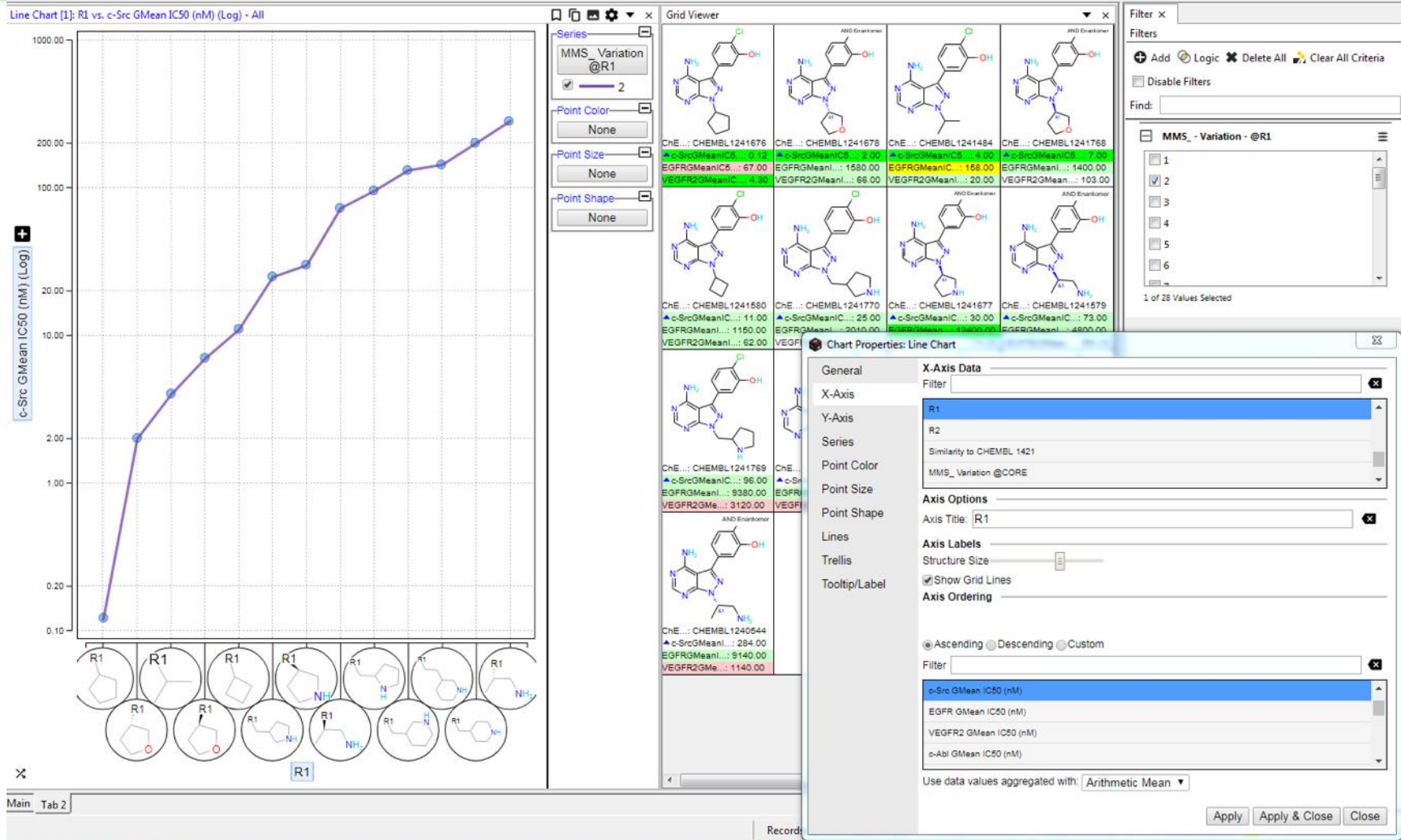
Point Color:

Point Size:

Point Shape:

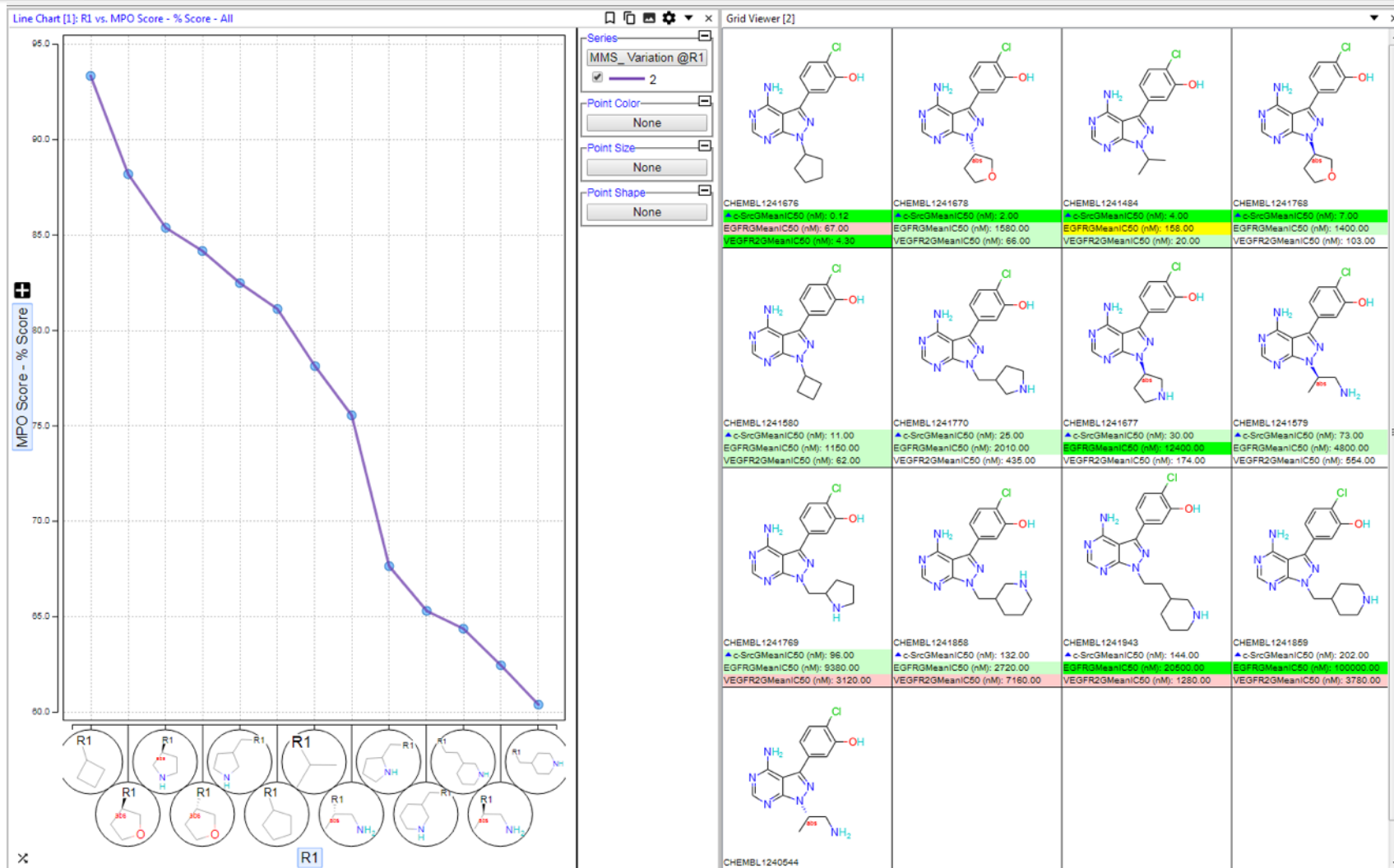
|   |  |  |  |
|---|--|--|--|
| <br>CHEMBL1241579<br>▲ c-SrcGMeanIC50 (nM): 73.00<br>EGFRGMeanIC50 (nM): 4800.00<br>VEGFR2GMeanIC50 (nM): 554.00    | <br>CHEMBL1241859<br>▲ c-SrcGMeanIC50 (nM): 202.00<br>EGFRGMeanIC50 (nM): 190000.00<br>VEGFR2GMeanIC50 (nM): 3780.00 | <br>CHEMBL1240544<br>▲ c-SrcGMeanIC50 (nM): 284.00<br>EGFRGMeanIC50 (nM): 9140.00<br>VEGFR2GMeanIC50 (nM): 1140.00 | <br>CHEMBL1241580<br>▲ c-SrcGMeanIC50 (nM): 11.00<br>EGFRGMeanIC50 (nM): 1150.00<br>VEGFR2GMeanIC50 (nM): 62.00  |
| <br>CHEMBL1241943<br>▲ c-SrcGMeanIC50 (nM): 144.00<br>EGFRGMeanIC50 (nM): 20500.00<br>VEGFR2GMeanIC50 (nM): 1280.00 | <br>CHEMBL1241676<br>▲ c-SrcGMeanIC50 (nM): 0.12<br>EGFRGMeanIC50 (nM): 67.00<br>VEGFR2GMeanIC50 (nM): 4.30          | <br>CHEMBL1241677<br>▲ c-SrcGMeanIC50 (nM): 30.00<br>EGFRGMeanIC50 (nM): 12400.00<br>VEGFR2GMeanIC50 (nM): 174.00  | <br>CHEMBL1241678<br>▲ c-SrcGMeanIC50 (nM): 2.00<br>EGFRGMeanIC50 (nM): 1580.00<br>VEGFR2GMeanIC50 (nM): 66.00   |
| <br>CHEMBL1241768<br>▲ c-SrcGMeanIC50 (nM): 7.00<br>EGFRGMeanIC50 (nM): 1400.00<br>VEGFR2GMeanIC50 (nM): 103.00     | <br>CHEMBL1241769<br>▲ c-SrcGMeanIC50 (nM): 96.00<br>EGFRGMeanIC50 (nM): 9380.00<br>VEGFR2GMeanIC50 (nM): 3120.00    | <br>CHEMBL1241484<br>▲ c-SrcGMeanIC50 (nM): 4.00<br>EGFRGMeanIC50 (nM): 158.00<br>VEGFR2GMeanIC50 (nM): 20.00      | <br>CHEMBL1241770<br>▲ c-SrcGMeanIC50 (nM): 25.00<br>EGFRGMeanIC50 (nM): 2010.00<br>VEGFR2GMeanIC50 (nM): 435.00 |
| <br>CHEMBL1241858<br>▲ c-SrcGMeanIC50 (nM): 132.00<br>EGFRGMeanIC50 (nM): 2720.00<br>VEGFR2GMeanIC50 (nM): 7160.00  |  |  |  |

# Exploring Activity Trends in Matched Molecular Series-Focus on One Series



- Order R1 by activity
- You can easily pick other series from the filter dialog
- You can easily switch to other properties from the Y-Axis

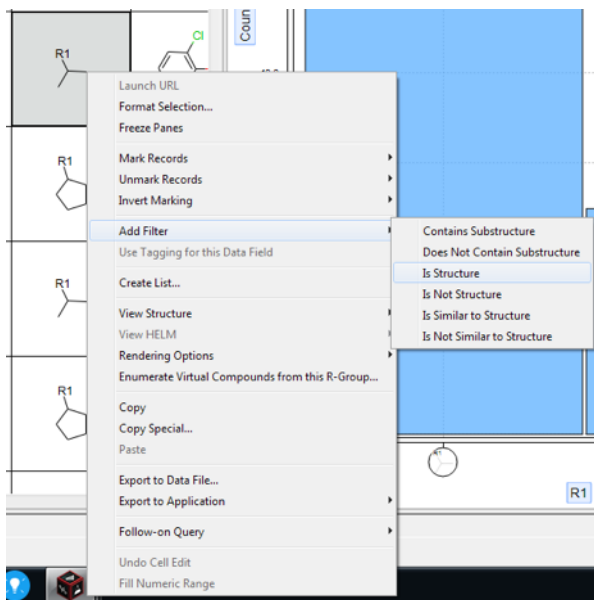
# Exploring Activity Trends in Matched Molecular Series-Focus on One Series-2



- Switched to MPO Score-Y-Axis
- Sorted R1 by MPO Score

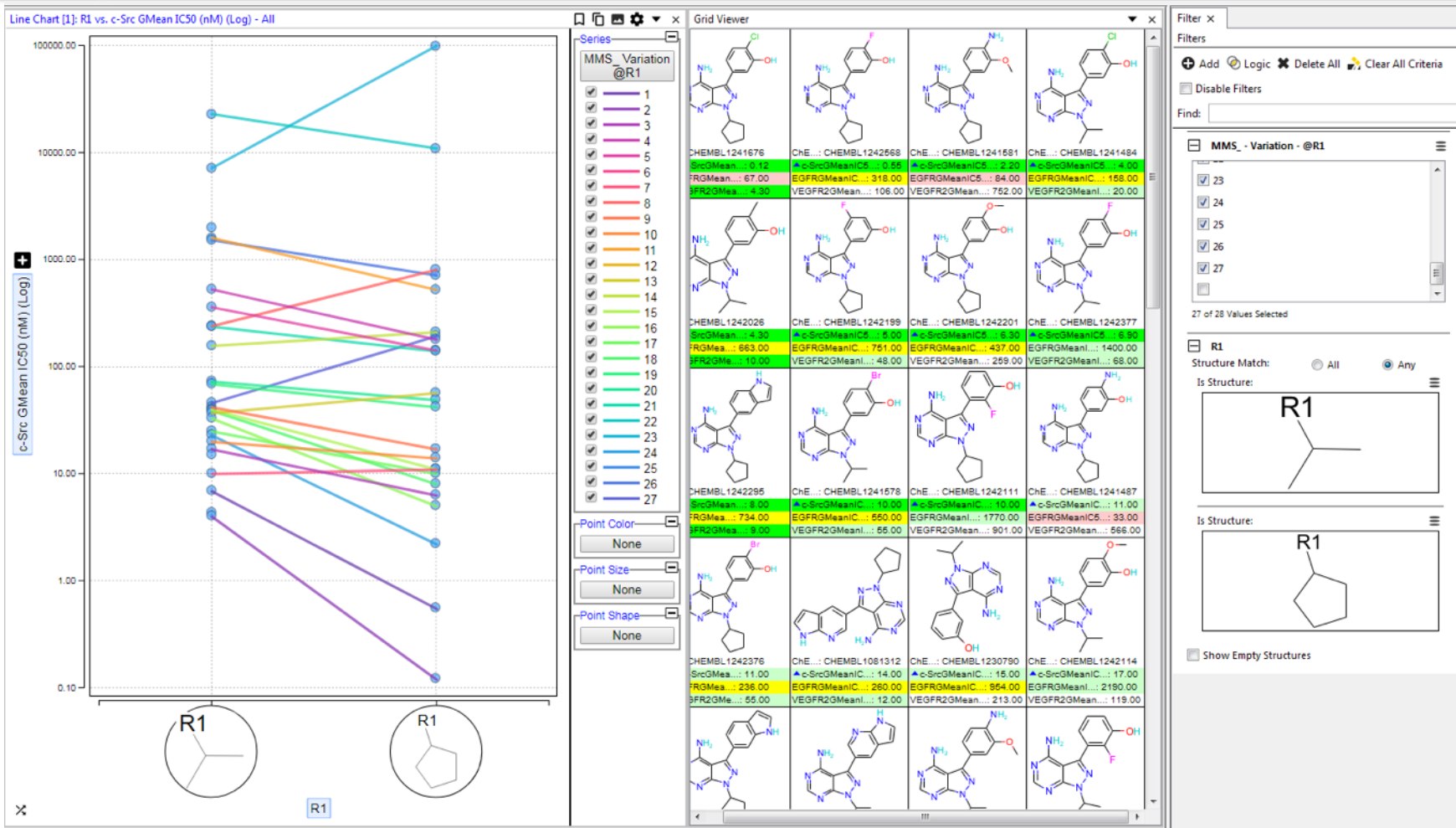
# Exploring Activity Trends in Matched Molecular Series-Focus on Two Fragments

- How does activity change when only one Fragment changes?



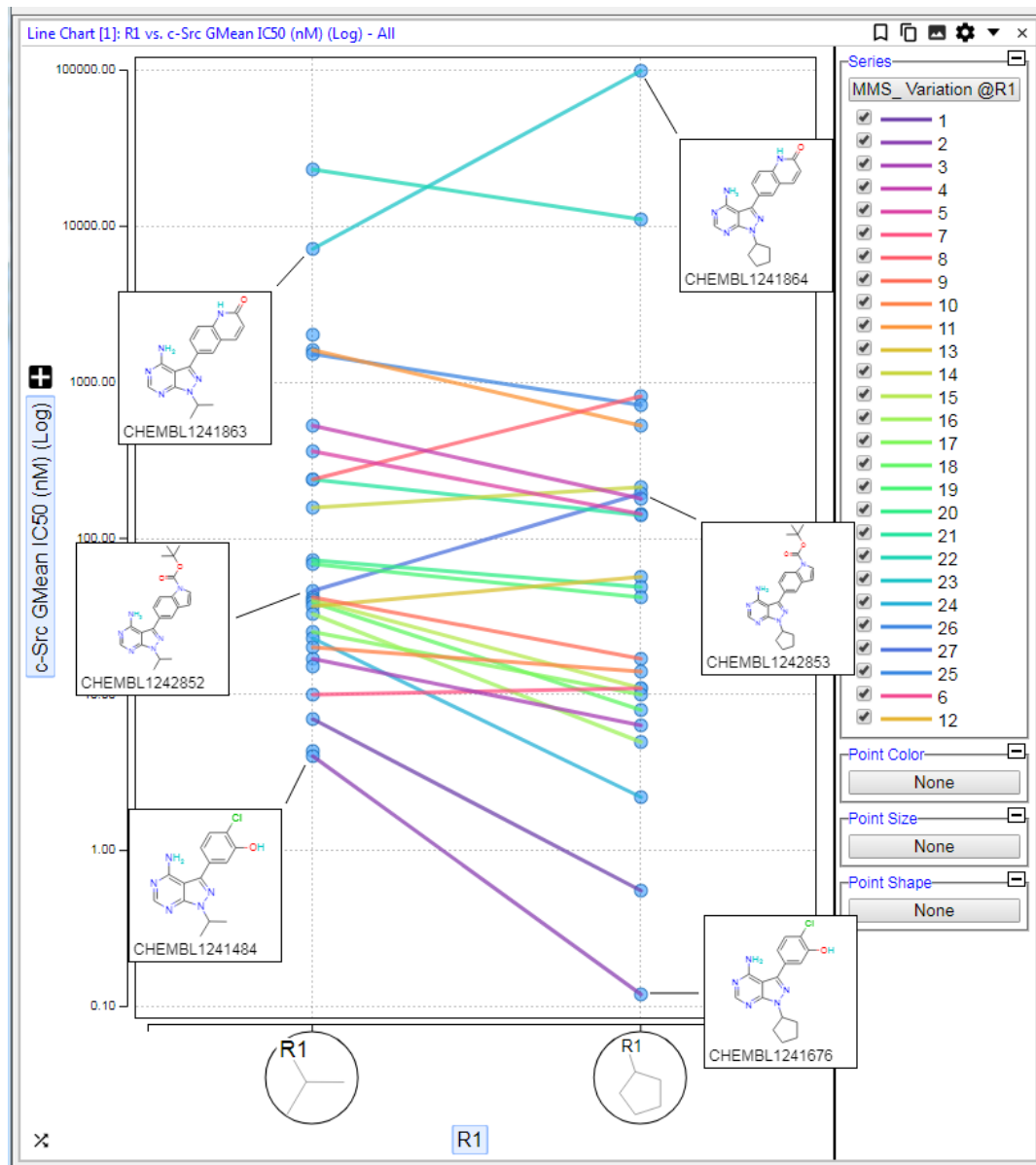
- Right click on one of the desired R1 fragments and select **Filter Is Structure**
- Disable this Filter Gadget
- Right click on another one of the desired R1 fragments and select **Filter Is Structure**
- Re-enable the first structure gadget and set the logic for this section to be "**Any**". This will find all compounds in the dataset that have either of these R1 fragments

# Exploring Activity Trends in Matched Molecular Series-Explore the Pairwise Results



- Clear indications of the effect of pair-wise changes in activity
- Easy to change activity (Y-Axis) or individual R-Group pairs

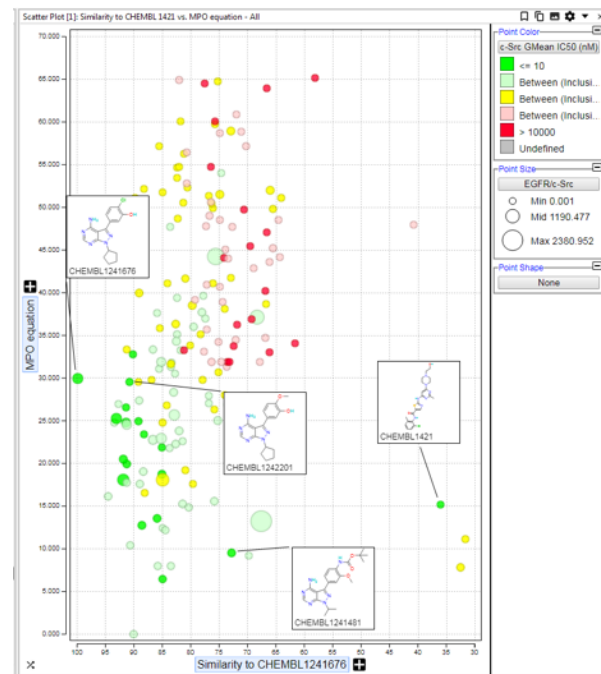
# Exploring Activity Trends in Matched Molecular Series-Explore the Pairwise Results



- For most of these pairs changing from isopropyl to cyclopentyl was beneficial, but for several pairs there was a dramatic decrease in activity

# Structure Similarity and MPO Scoring-Looking for Interesting Outliers

- How do changes in the overall structure for a series of compounds affect activity?
  - Structure Similarity Maps give an overall view of all the structures along with activity data
- How does the activity vary with Similarity to a single compound?



# Structure Similarity and MPO Scoring-Looking for Interesting Outliers-Setup

- Pick the Compound in your current dataset to focus on (e.g. ChEMBL 1241676)
  - This might be the most potent compound in your primary assay or the one with the best overall profile
- Create a Similarity equation
- Create a Multi-Parameter Score for your desired profile

Equation:

Multi-Parameter Scoring

Information  
Multi-Parameter Scoring assesses the quality of substances relative to each other by balancing the values of various molecular properties in a single overall scoring function.

MPO Score Criteria

Filter Data Fields:

| Data Field              | Function         | Weig... |
|-------------------------|------------------|---------|
| c-SrcGMeanIC50 (nM)     | Low Values Good  | 2       |
| EGFRGMeanIC50 (nM)      | High Values Good | 1       |
| VEGFR2GMeanIC50 (nM)    | Low Values Good  | 1       |
| PIBKbetaGMeanIC50 (nM)  | High Values Good | 1       |
| PIBKdeltaGMeanIC50 (nM) | High Values Good | 1       |

Add scores as a % of the max scores  
 Add raw scores  
 Add scoring function max scores

Column Prefix:

Calculate Scores Cancel



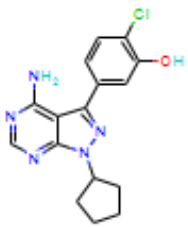
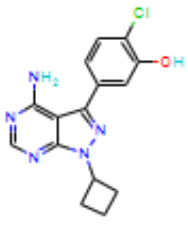
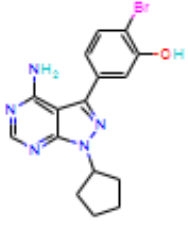

# Structure Similarity and MPO Scoring-Looking for Interesting Outliers-Setup-2

- Create an equation to show the MPO scores of all compounds relative to my reference compound

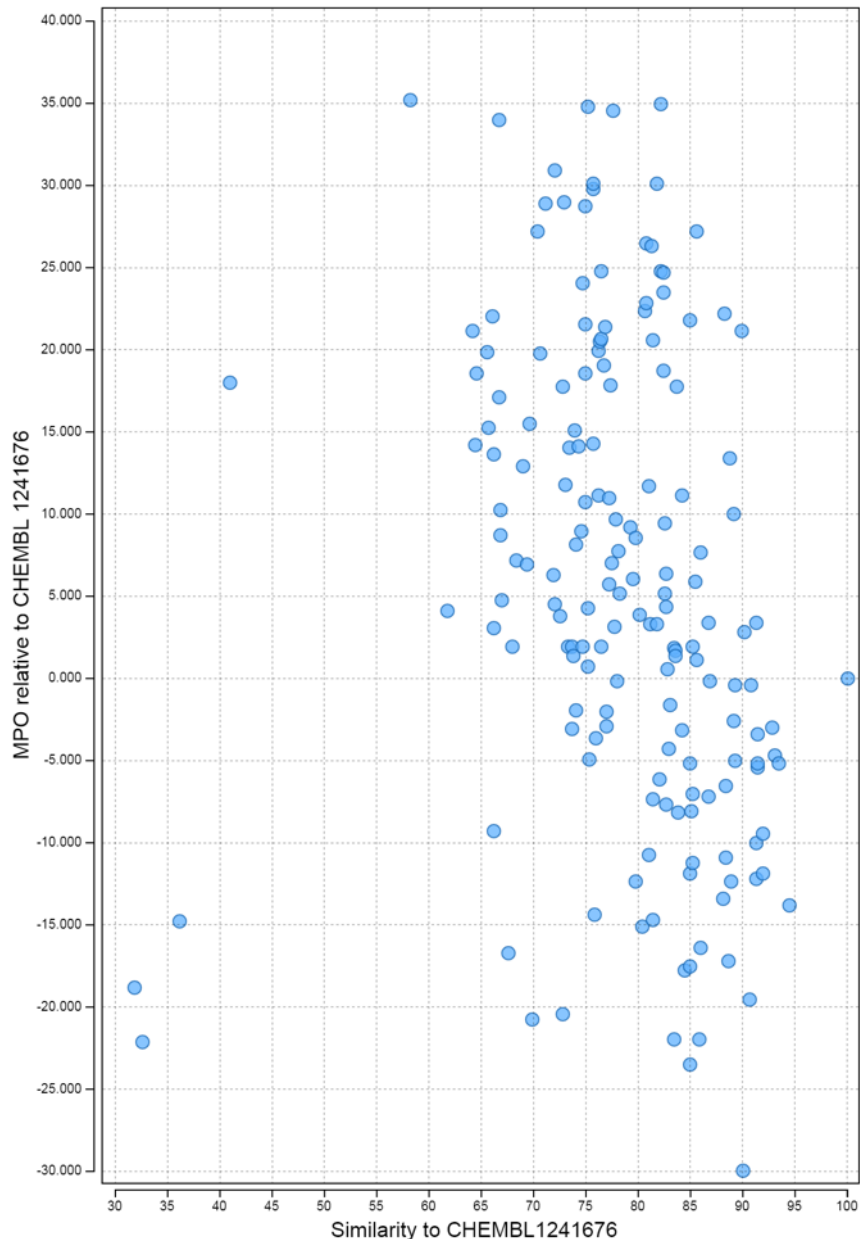
Equation:

51.9-C28

Spreadsheet

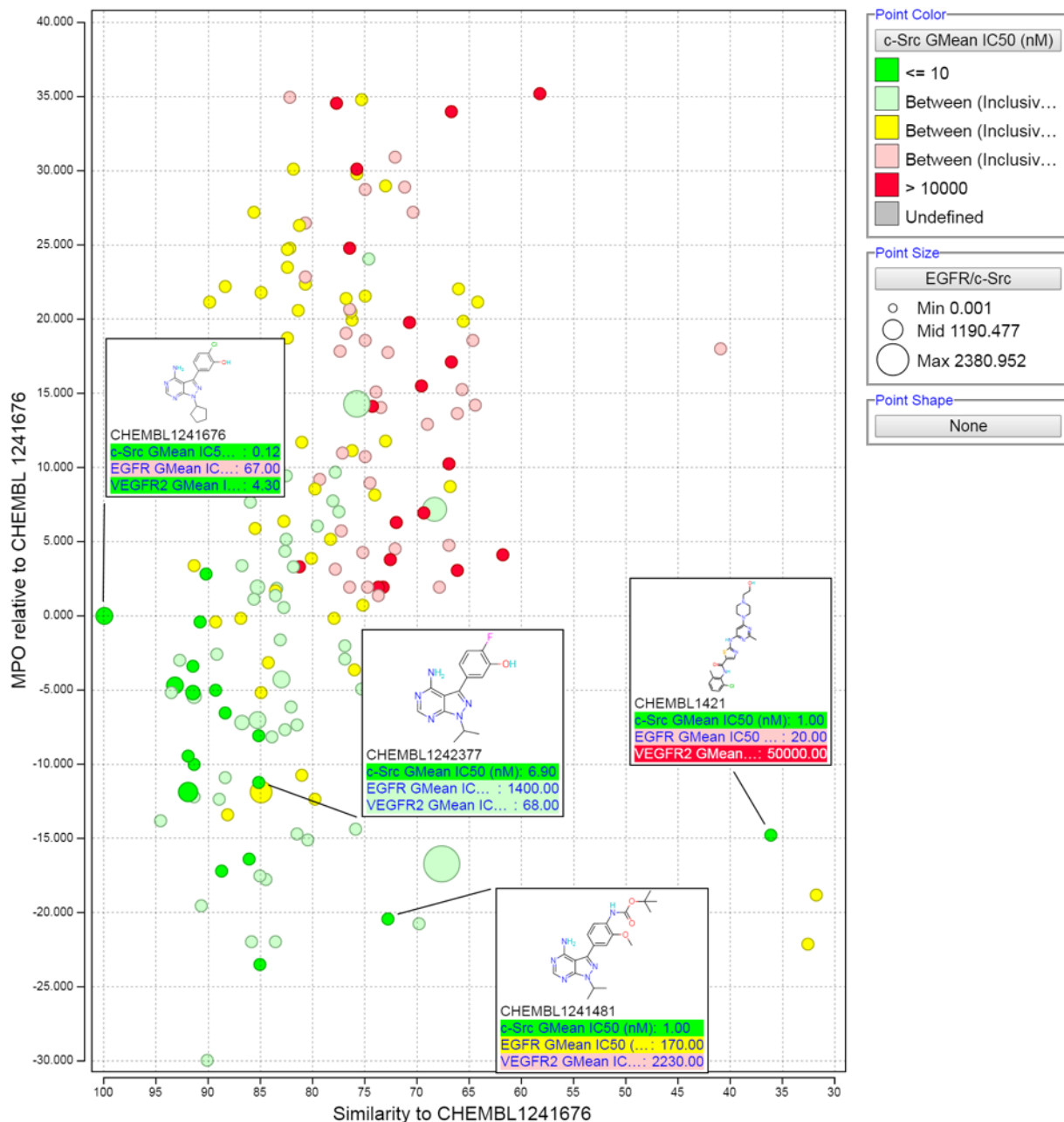
|    | ChEMBL Id                              | Structure   | Similarity to CHEMBL1241676 | MPO Score - % Score | MPO relative to CHEMBL 1241676 |
|----|--|---|-----------------------------|---------------------|--------------------------------|
| 1: | <input type="checkbox"/> CHEMBL1241676 |    | 100                         | 51.9                | -0.00                          |
| 2: | <input type="checkbox"/> CHEMBL1241580 |   | 95                          | 65.7                | -13.84                         |
| 3: | <input type="checkbox"/> CHEMBL1242376 |  | 93                          | 57.0                | -5.14                          |
|    |  |  |                             |                     |                                |

# Structure Similarity and MPO Scoring-Looking for Interesting Outliers-Scatterplot



- Reverse the axis for the Similarity Score (X-Axis)
- Add in Point color for the primary assay
- Add in point size for a EGFR/c-Src selectivity value
- Add some assays to the tooltip
- Add in some sticky labels (v20.1!)

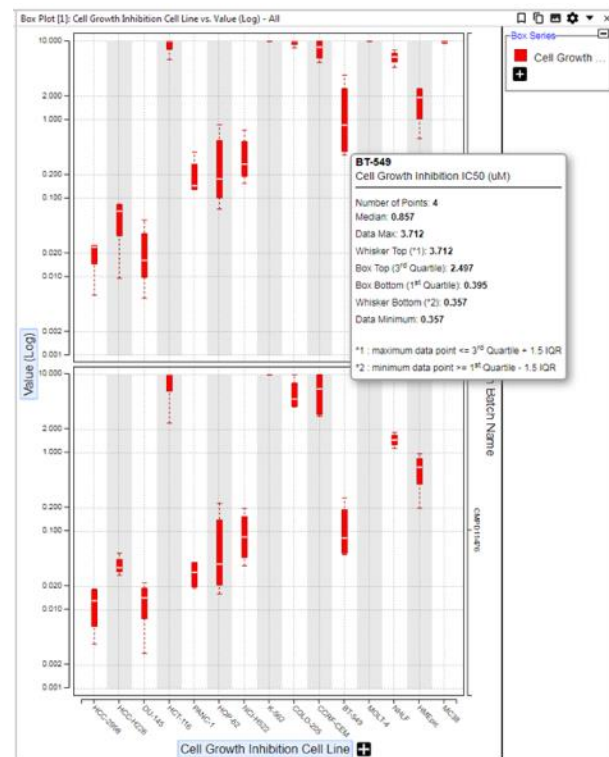
# Structure Similarity and MPO Scoring-Looking for Interesting Outliers-Scatterplot tuned



- **Compounds that are similar in structure to the target that have a much lower MPO?**
- **Compounds that are not similar to the target compound that have good, if not better MPO?**

# Exploring Assay Performance with Selected Compounds

- There are several ways to see how your compounds are behaving in assays:
  - Dose Response Curves
  - Statistical aggregation types like standard deviation and confidence intervals as columns to your dataset
  - Looking at the in cell indicators for the clues about the underlying unaggregated data
- Several other assay performance analyses you might want to do:
  - How standards perform in assays over time
  - Reproducibility of compounds across assays



# Exploring Assay Performance with Selected Compounds-Standards-setup

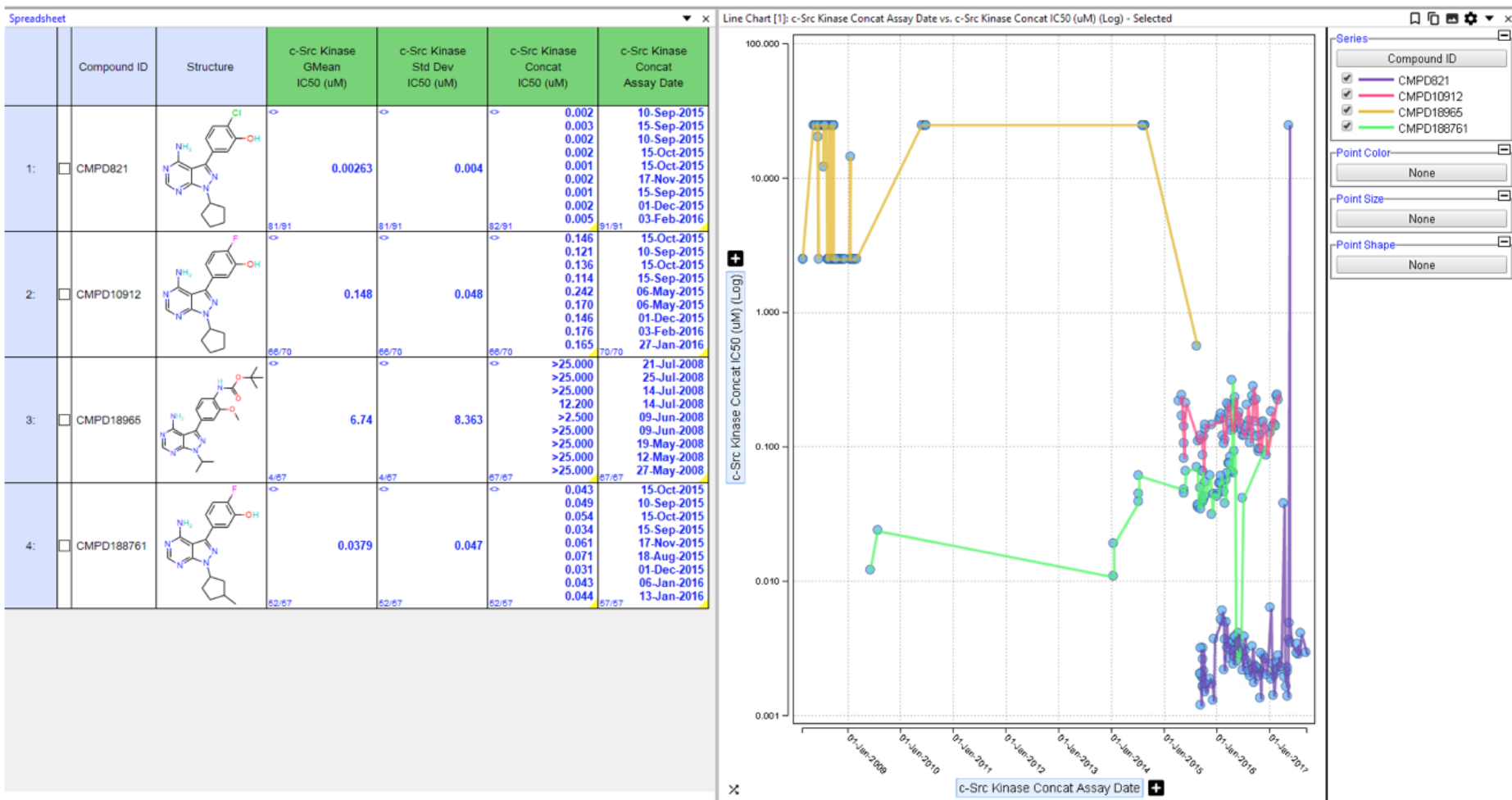
- Compound ID (constrained by 4 compound IDs)
- Structure (if desired)
- Assay that is under review (e.g. c-Src Kinase)
  - Include the summarized value (e.g. IC50) with the aggregation functions GMean and Concatenate LF and Standard Deviation.
  - Include the date the experiment was run with the aggregation function of Concatenate LF.

| Spreadsheet |                                     |           |                                    |                                      |   |   |
|-------------|-------------------------------------|-----------|------------------------------------|--------------------------------------|---|---|
|             | Compound ID                         | Structure | c-Src Kinase<br>GMean<br>IC50 (uM) | c-Src Kinase<br>Std Dev<br>IC50 (uM) | c-Src Kinase<br>Concat<br>IC50 (uM)   | c-Src Kinase<br>Concat<br>Assay Date  |
| 1:          | <input type="checkbox"/> CMPD821    |           | 0.00263                            | 0.004                                | 0.002<br>0.003<br>0.002<br>0.002<br>0.001<br>0.002<br>0.001<br>0.002<br>0.005                 | 10-Sep-2015<br>15-Sep-2015<br>10-Sep-2015<br>15-Oct-2015<br>15-Oct-2015<br>17-Nov-2015<br>15-Sep-2015<br>01-Dec-2015<br>03-Feb-2016 |
| 2:          | <input type="checkbox"/> CMPD10912  |           | 0.148                              | 0.048                                | 0.146<br>0.121<br>0.136<br>0.114<br>0.242<br>0.170<br>0.146<br>0.176<br>0.165                 | 15-Oct-2015<br>10-Sep-2015<br>15-Oct-2015<br>15-Sep-2015<br>06-May-2015<br>06-May-2015<br>01-Dec-2015<br>03-Feb-2016<br>27-Jan-2016 |
| 3:          | <input type="checkbox"/> CMPD18965  |           | 6.74                               | 8.363                                | >25.000<br>>25.000<br>>25.000<br>12.200<br>>2.500<br>>25.000<br>>25.000<br>>25.000<br>>25.000 | 21-Jul-2008<br>25-Jul-2008<br>14-Jul-2008<br>14-Jul-2008<br>09-Jun-2008<br>09-Jun-2008<br>19-May-2008<br>12-May-2008<br>27-May-2008 |
| 4:          | <input type="checkbox"/> CMPD188761 |           | 0.0379                             | 0.047                                | 0.043<br>0.049<br>0.054<br>0.034<br>0.061<br>0.071<br>0.031<br>0.043<br>0.044                 | 15-Oct-2015<br>10-Sep-2015<br>15-Oct-2015<br>15-Sep-2015<br>17-Nov-2015<br>18-Aug-2015<br>01-Dec-2015<br>06-Jan-2016<br>13-Jan-2016 |

# Exploring Assay Performance with Selected Compounds-Standards-Line Chart

- Add a Line Chart

- X-Axis is date the experiment was run (concat LF)
- Y-Axis is Assay IC60 (concat LF). Set this axis to be log scaled
- Set the Line Series up to use the Compound ID column



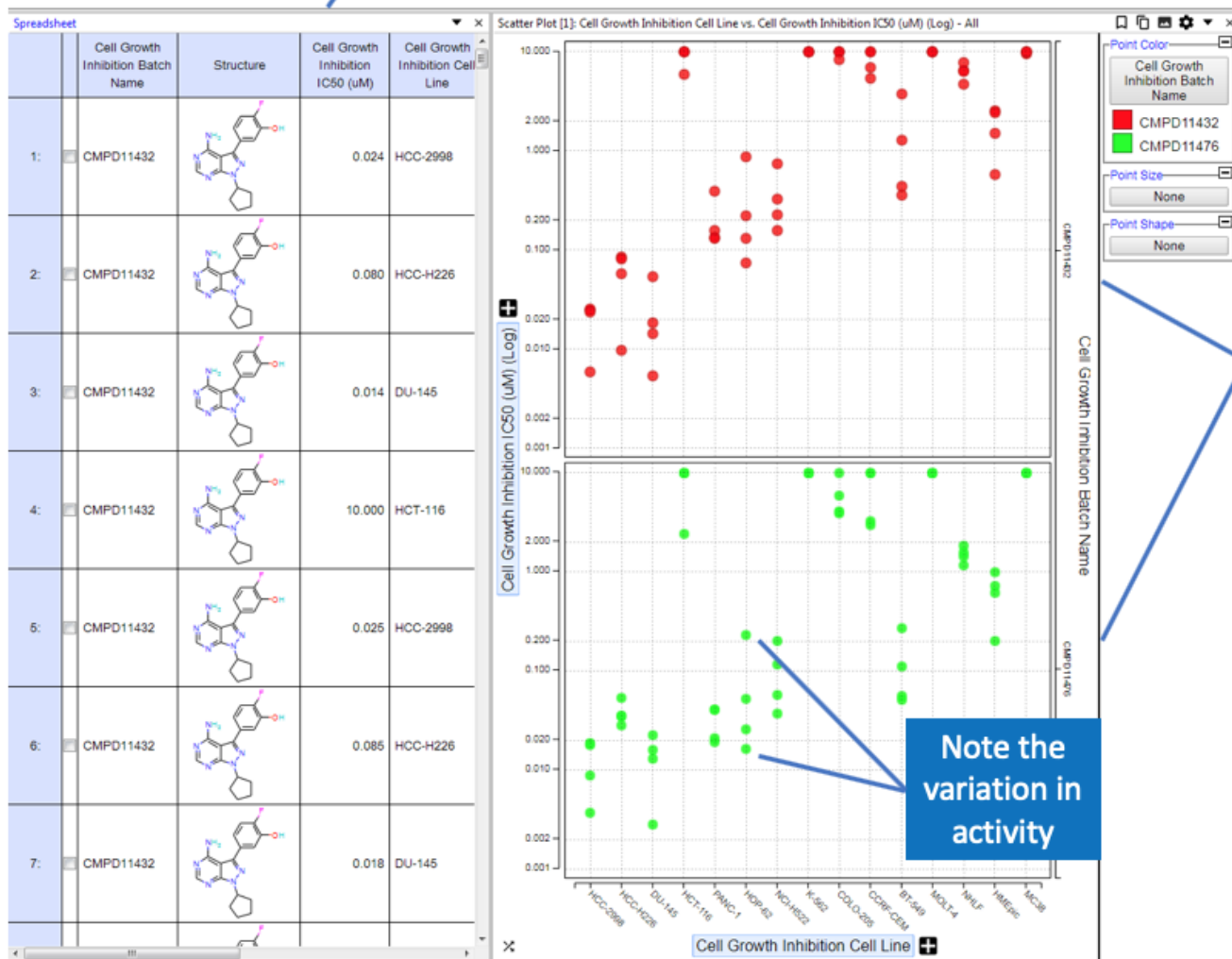
- In assay development or quality control you might want to see how multiple measurements during the same run look for your compounds
- While it is easy to add in statistical fields like Standard Deviation, Min, Max... it is sometimes easier to just visualize it

### Setup

- Compound ID (constrained by two compound IDs)
- Structure
- Assay that is under review (e.g. Cell growth Inhibition)
  - Desired result type (e.g. **IC50**) and set the cell line condition to be **unpivoted**
  - Include the Analysis fields **Batch Name** and **Experiment Date**
  - Constrain the Experiment date to a date or set of dates to review
  - Set the query to run as **Unaggregated**

# Exploring Assay Performance with Selected Compounds-Scatter Graph

Unaggregated,  
not pivoted dataset

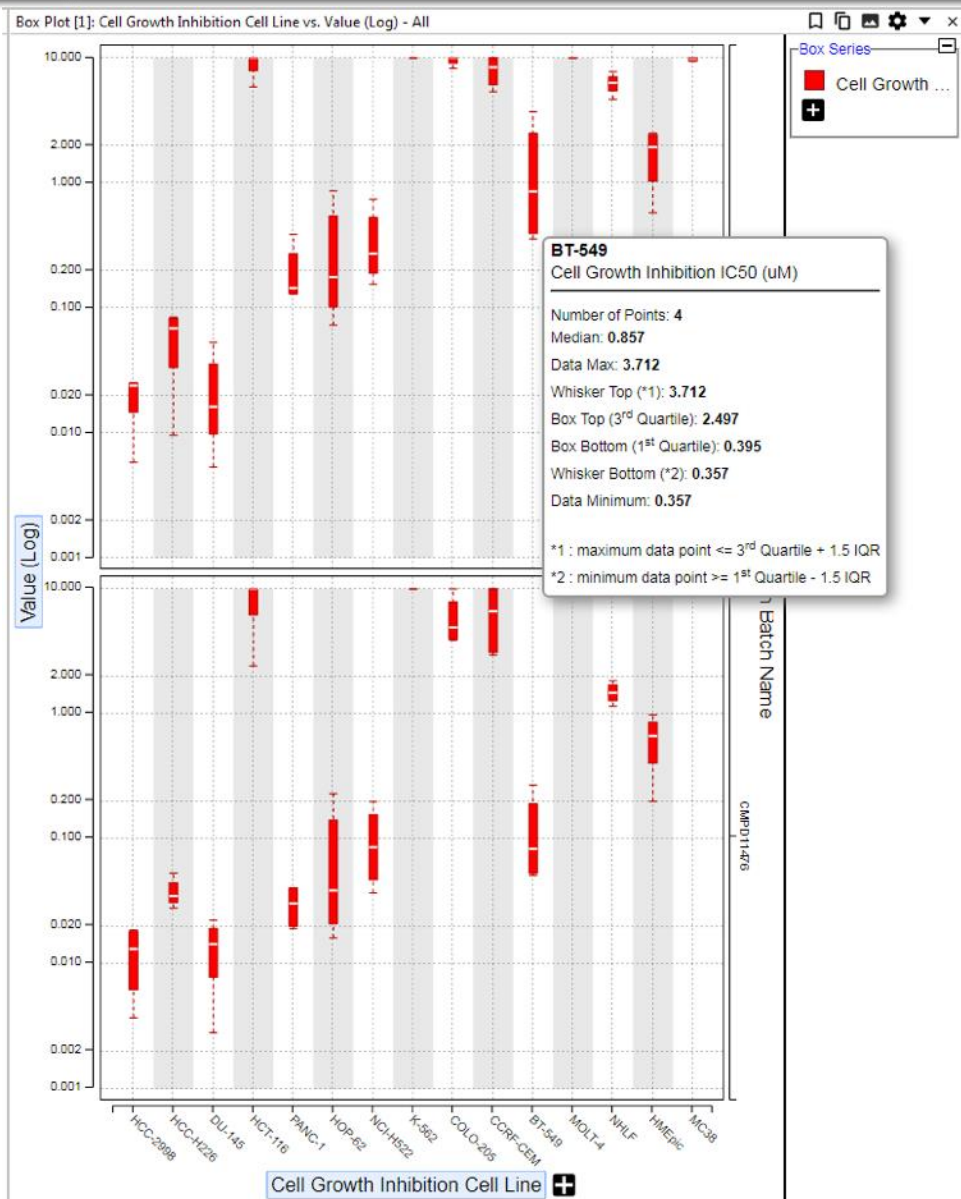


Trellised and  
point color by  
Batch Name

Note the  
variation in  
activity



# Exploring Assay Performance with Selected Compounds-Box Plot



- **Box Plots** give a quick visual indication of data range
- **Tooltips** afford all the detailed statistics for the **Box (and Whisker)**

# Follow On Queries-not just for Administrators

- Most organizations have Follow On Queries (FOQ) as standard templates for common workflows
- Often overlooked is the ability for any user to create FOQs for personal or project use

|       |          |           |          |          |          |
|-------|----------|-----------|----------|----------|----------|
| 1/1   | 1/1      | 1/1       | 1/1      | 1/1      | 1/1      |
| 1.0E3 | 1.00     | 1900.00   | 1200.00  | 110.00   | 50000.00 |
| 70E4  | 50000.00 | 50000.00  | 17000.00 | 50000.00 | 9600.00  |
| 50E4  | 10000.00 | 100000.00 |          |          |          |

- Format Selection...
- Freeze Panes
- Mark Records
- Unmark Records
- Invert Marking
- Add Filter
- Use Tagging for this Data Field
- Create List...
- View Structure
- View HELM
- Rendering Options
- Copy
- Copy Special...
- Paste
- Export to Data File...
- Export to Application
- Follow-on Query
  - Compound Report Card
  - Compound Details
  - Show Assays Tested in Compound(s)
  - Cross Target Summary
  - Personal
  - 10 Demos
  - Oncology Project

- Bullseye
- Kinase Project Rgroup 10 Demo
- Kinase Project Rgroup FW vis
- Kinase Project Rgroup SP2
- Kinase Project Rgroup SP2 MPO test
- Kinase Project Rgroup SP2 MPO test 191
- Kinase Project Rgroup SP3
- Marketed compounds form 100
- Marketed compounds form wrap

Any query can be an FOQ that

- Has a Domain-able field (e.g. Compound ID) or a structure field exposed in the widget
- Is saved as a widget
- Is visible on the Dashboard

# KnowledgeBase Articles-where to find these workflows!

## • Virtual Compounds in D360

- [An Overview of Virtual Compounds](#)
- [Adding Virtual Compounds to a D360 Dataset](#)
- [Enumerating Virtual Compounds from R-groups and Cores](#)
- [Deleting Virtual Compounds from a D360 Dataset](#)
- [Creating a D360 Dataset from a Chemical Structure File or Sketch](#)
- [Capturing Virtual Compounds](#)

## • Exporting Data

- [Exporting Data to Excel](#)
- [Exporting Data to Data Files - csv, tsv, sdf, xls, xlsx, json](#)
- [Exporting Data to PowerPoint](#)
- [Copying Data to the Clipboard](#)

## • Miscellaneous

- [D360 URL execution of query templates](#)
- [Installing D360 on a Windows PC](#)
- [Installing D360 on a Mac](#)
- [How to Specify Chiral Information in Commonly used Chemical Sketchers](#)
- [Test Automation Tool](#)

## • Tips and Tricks for Small Molecule Discovery

- [Exploring Activity Trends in Matched Molecular Series](#)
- [Structure Similarity and Multi-Parameter Scoring - Looking for Interesting Outliers](#)
- [Exploring Assay Performance with Selected Compounds](#)
- [Bioprofile Summary Results](#)

## • D360 Partner - A D360 Client for External Research Partners

- [D360 Partner - An Overview of Sharing Data with External Research Partners](#)
- [D360 Partner setup for Administrators](#)
- [D360 Partner Query setup](#)
- [D360 Partner Use](#)

# Acknowledgements

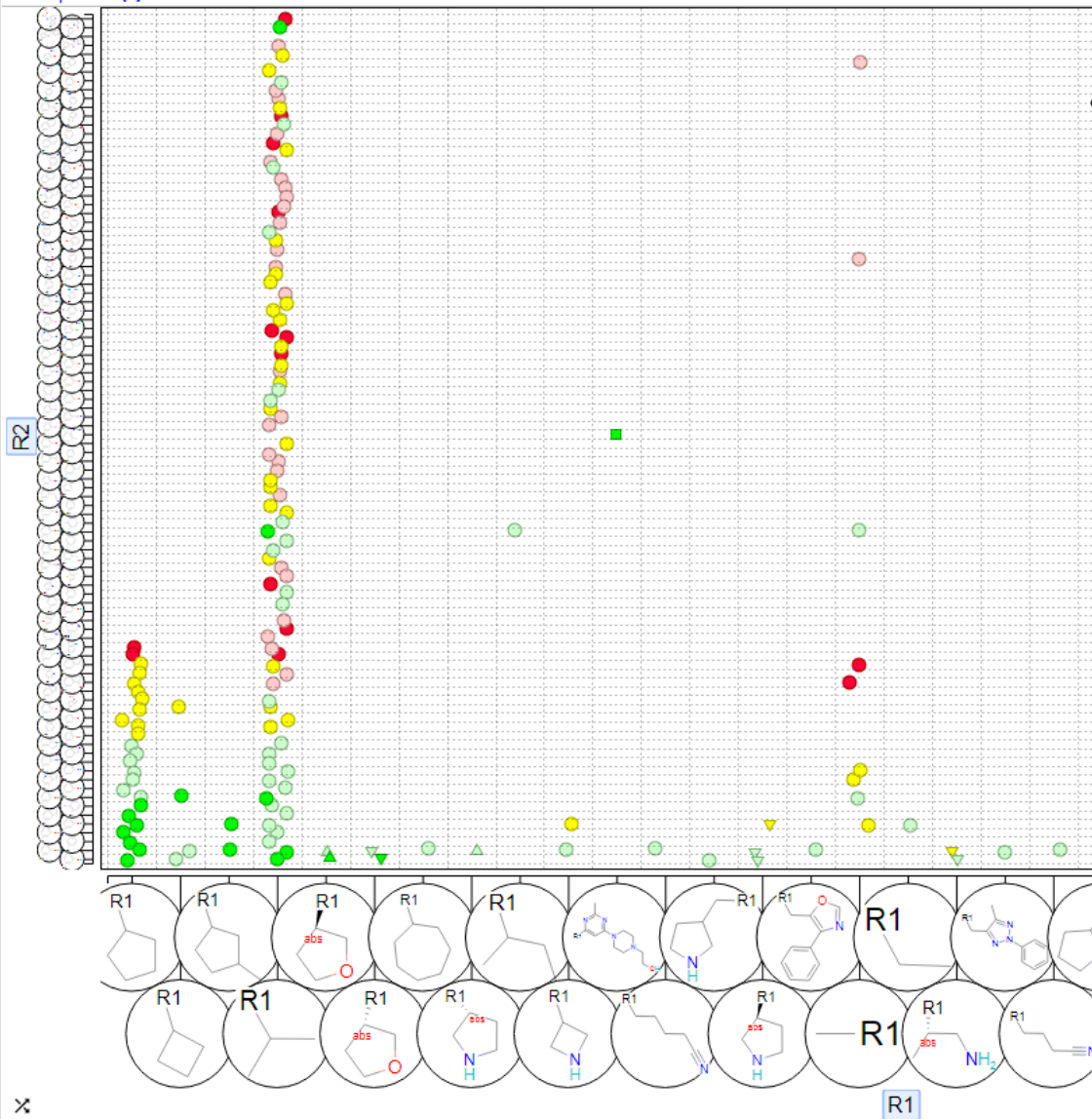
- Exploring Activity Trends in Matched Molecular Series
  - John Cummings (Roche), Lars Burgdorf (Merck KGaA), Dietrich Boese (Merck KGaA)
- Exploring Assay Performance with Selected Compounds
  - Beverley Smith (Medimmune)
- Favorite tools
  - Justin Montgomery (Pfizer)
- Certara Folks
  - David Lewis, and the Development Team for giving me all the tools...

# One More Thing...R-Group Activity Contribution Analysis

- Modeling the contribution of each R-Group fragment to any activity could lead to a better understanding of the SAR for the series
- With a good model in hand, you should be able to Predict the activity of Virtual compounds
- This would augment the services that several companies have with virtual assays.

# R-Group Activity Contribution Analysis – Setup

R-Group Matrix [1]: R1 vs. R2 - All

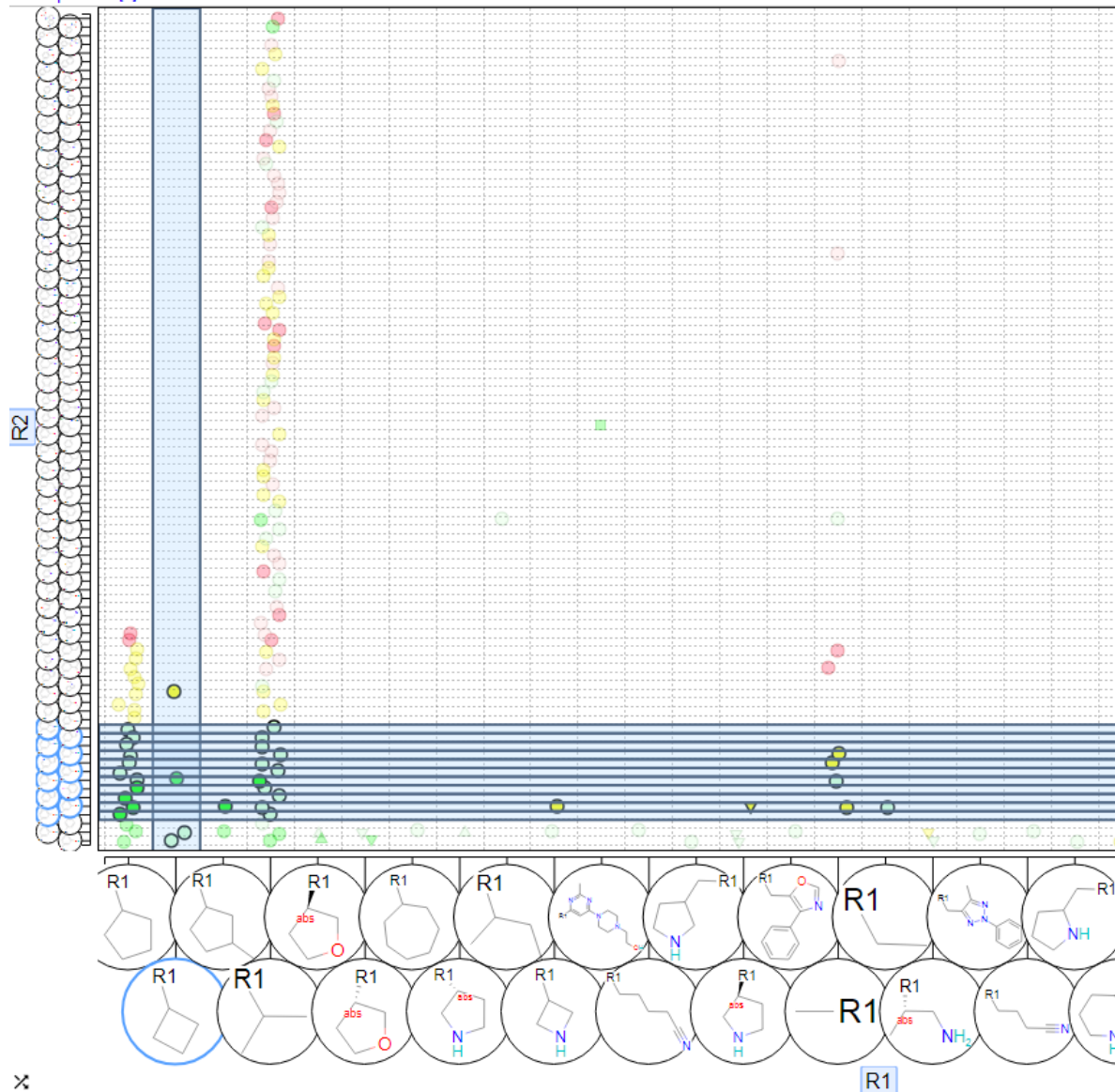


## R-Group Matrix

- R1 sorted by Min c-Src activity
- R2 sorted by first fragment c-Src activity

# R-Group Activity Contribution Analysis – Virtual Compounds 1

R-Group Matrix [1]: R1 vs. R2 - All



## Virtual Compounds

- Selected the section where expected activity might be found

# R-Group Activity Contribution Analysis – Virtual Compounds 2

- **Virtual Compounds**
  - Enumerated the Compounds

Enumerate Virtual Compounds from R-Groups

Information:

- Select Core and R-Group structures from their respective tabs.
- Specify filters to limit structures that are enumerated.
- Click "Create Structures" when complete.

Core (1 of 4) | R1 (1 of 33) | R2 (11 of 96) | Product Structure Filters (0)

Select All | Invert Sel

|                                     | R2 | Frequenc |
|-------------------------------------|----|----------|
| <input checked="" type="checkbox"/> |    |          |
| <input checked="" type="checkbox"/> |    |          |
| <input checked="" type="checkbox"/> |    |          |
| <input checked="" type="checkbox"/> |    |          |
| <input checked="" type="checkbox"/> |    |          |
| <input checked="" type="checkbox"/> |    |          |

Group selection will create 11 new structures



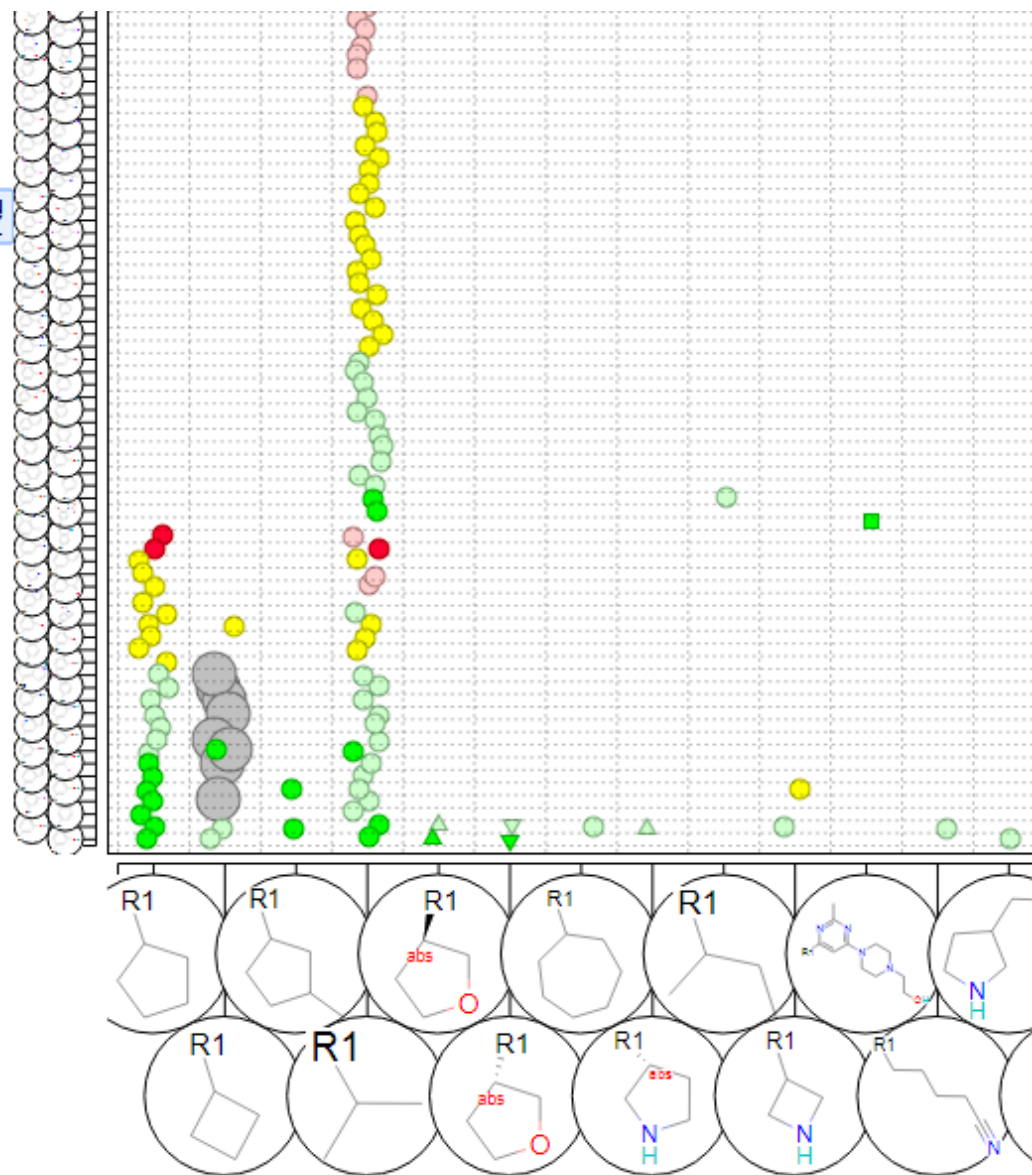
Enumerated Structure Selector

# Columns  | Select All | Invert Selection | Clear Selection

|                                     |  |                                     |  |                                     |  |
|-------------------------------------|--|-------------------------------------|--|-------------------------------------|--|
| <input checked="" type="checkbox"/> |  | <input checked="" type="checkbox"/> |  | <input checked="" type="checkbox"/> |  |
| <input checked="" type="checkbox"/> |  | <input checked="" type="checkbox"/> |  | <input checked="" type="checkbox"/> |  |
| <input checked="" type="checkbox"/> |  | <input checked="" type="checkbox"/> |  | <input checked="" type="checkbox"/> |  |
| <input checked="" type="checkbox"/> |  | <input checked="" type="checkbox"/> |  |                                     |  |



# R-Group Activity Contribution Analysis – Virtual Compounds 3



- R-Group Matrix
  - New Virtual Compounds are highlighted with larger size and no activity

# R-Group Activity Contribution Analysis – Analysis Setup

Project Rgroup SP2 [1]

Viewers Analysis Data Virtual Compounds Quick Search Window Help

Quick Color

Color by Value...

Clear Coloring

Multi-Parameter Scoring

Highlight Updated Assay Data

R-Group Analysis...

R-Group Activity Contribution Analysis...

Correlation Matrix...

Statistics...

| VEGFR2   | c-Abl     | HCK       |
|----------|-----------|-----------|
| GMean    | GMean     | GMean     |
| C50 (nM) | IC50 (nM) | IC50 (nM) |

- R-Group Activity Contribution Analysis (v20.1)

Model Molecular Properties from R-Groups

Information

Modeling molecular properties employs the Free-Wilson method to determine contributions of various substituents to a chosen molecular property or biological activity.

You can choose to produce independent models each core from an R-Group analysis or to generate a single model employing the core as a site of variation.

Structures with R-groups that are unique to that structure cannot be included in the model. If a core structure is associated with > 10 structures then these structures will have a model created for them.

On completion of the calculation you will be presented with information that will tell you whether a valid model was created.

One model per core structure

One model overall (considering core as a site of variation)

Select Single Property to Model:

Filter:   Show hidden columns

- c-SrcGMeanIC50 (nM)
- EGFRGMeanIC50 (nM)
- VEGFR2GMeanIC50 (nM)
- c-AblGMeanIC50 (nM)
- HCKGMeanIC50 (nM)
- PI3KalphaGMeanIC50 (nM)

Log scale property

Create R-Group Contribution Models Cancel


# R-Group Activity Contribution Analysis – Analysis Setup - 2

- **Good Model with low standard error**

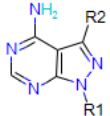

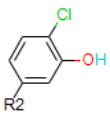
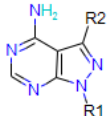

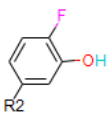
Model Browser

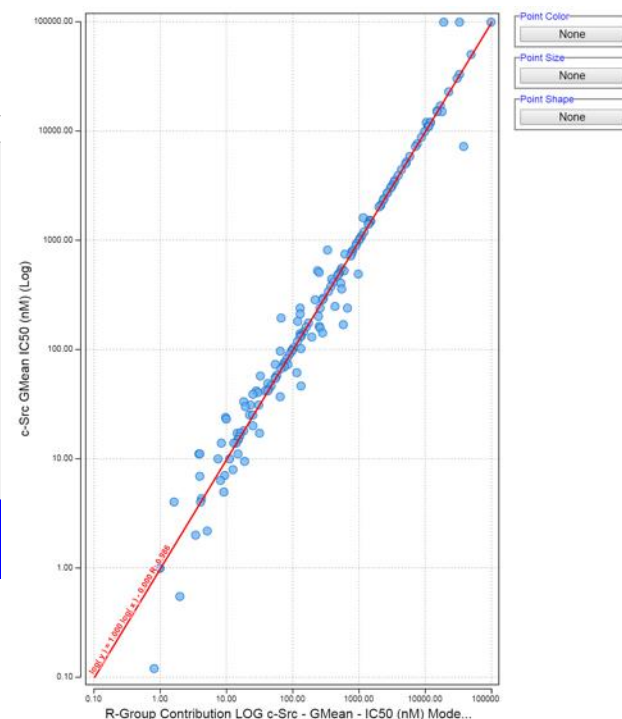
Properties Modeled: LOG c-Src - GMean - IC50 (nM) Delete Selected Models for this Property Delete all Models for this Property

Model Information

| Core  | # Obs | Interpretation | % Variance Explained (r-squared) | Standard Error | % Probability of Chance Model (Significance F) |
|---|-------|----------------|----------------------------------|----------------|--|
|  | 167   | 1 Good Model   | 97.2                             | 0.38           | 2.1  |



| Category | CORE   | R1  | R2  | R-Group Contribution LOG c-Src - GMean - IC50 (nM) CORE Contribution | R-Group Contribution LOG c-Src - GMean - IC50 (nM) R1 Contribution | R-Group Contribution LOG c-Src - GMean - IC50 (nM) R2 Contribution | R-Group Contribution LOG c-Src - GMean - IC50 (nM) Modeled Value |
|----------|--|---|---|--|--|--|--|
| Standard |    |    |    | 1.78   | -2.07  | 0.20   | 0.81   |
| Standard |  |  |  | 1.78   | -2.07  | 0.59   | 1.99   |



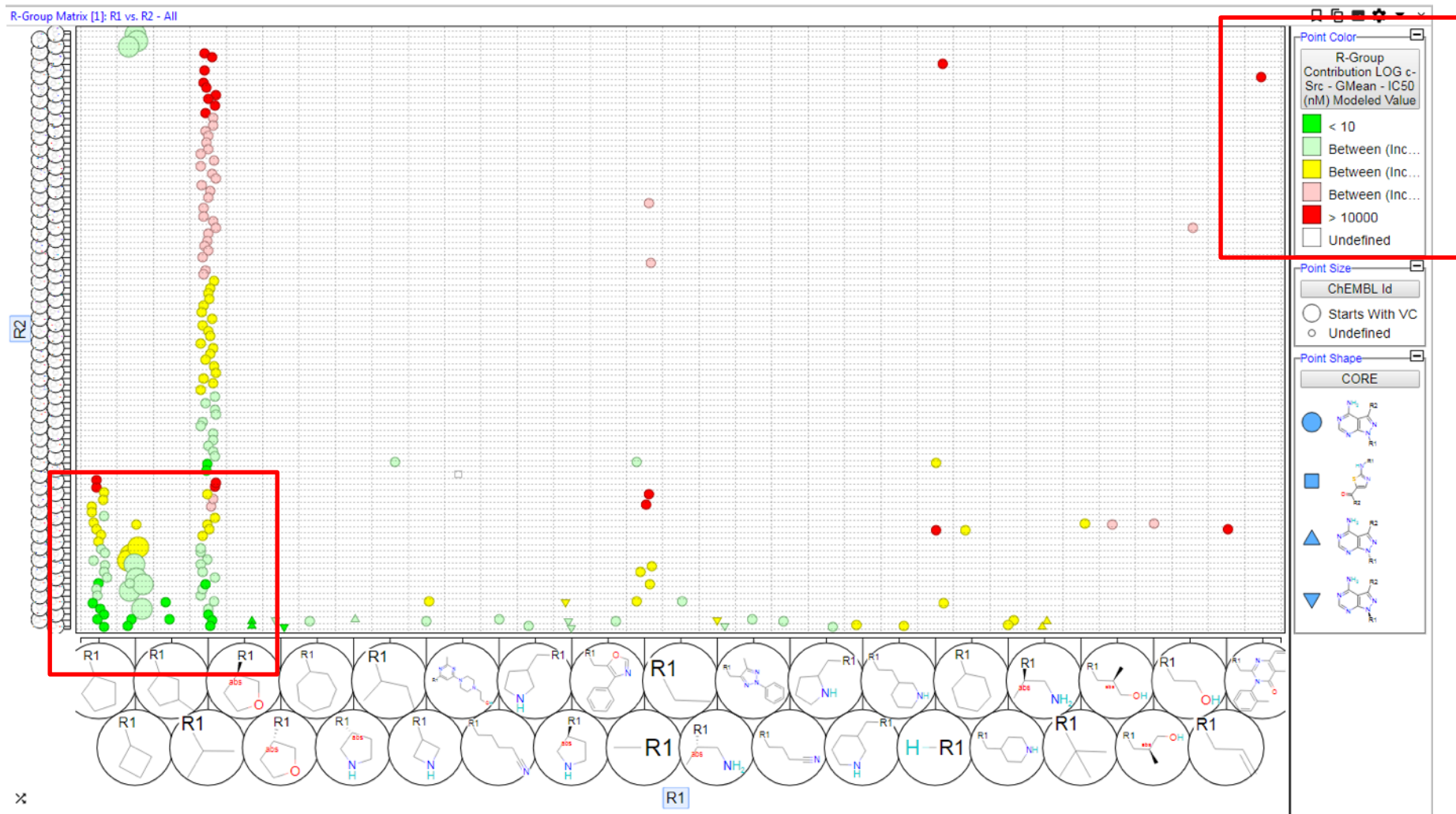
# R-Group Activity Contribution Analysis – Predict!

- With a good model in place lets predict the activity of the Virtual Compounds

The screenshot shows a software window titled "Data View: Free Wilson slides [1]". The menu bar includes File, Edit, Format, Viewers, Analysis, Data, Virtual Compounds, Quick Search, Window, and Help. The Analysis menu is open, showing options like Quick Color, Color by Value..., Clear Coloring, Multi-Parameter Scoring, Highlight Updated Assay Data, R-Group Analysis..., R-Group Activity Contribution Analysis..., Correlation Matrix..., and Statistics... The R-Group Activity Contribution Analysis... option is selected, opening a sub-menu with Create Property Model from R-Groups..., View Models..., and Predict... The background shows a spreadsheet with columns for ChEMBL Id, VEGFR2 GMean IC50 (nM), c-Abl GMean IC50 (nM), HCK GMean IC50 (nM), and PI3K GM IC50. Two rows are visible: row 177 with ChEMBL Id VC~0000006 and row 178 with ChEMBL Id VC~0000007. Chemical structures are shown in the third column for rows 177 and 178.

# R-Group Activity Contribution Analysis – New RGM

- R-Group Matrix with the Point Color by Model Predicted Activity



# R-Group Activity Contribution Analysis – New Targets for Synthesis

- **Virtual Compounds with Modeled Predicted Activity...**
- **Filtering by this predicted activity for the Virtual Compounds affords good candidates for Synthesis**

