



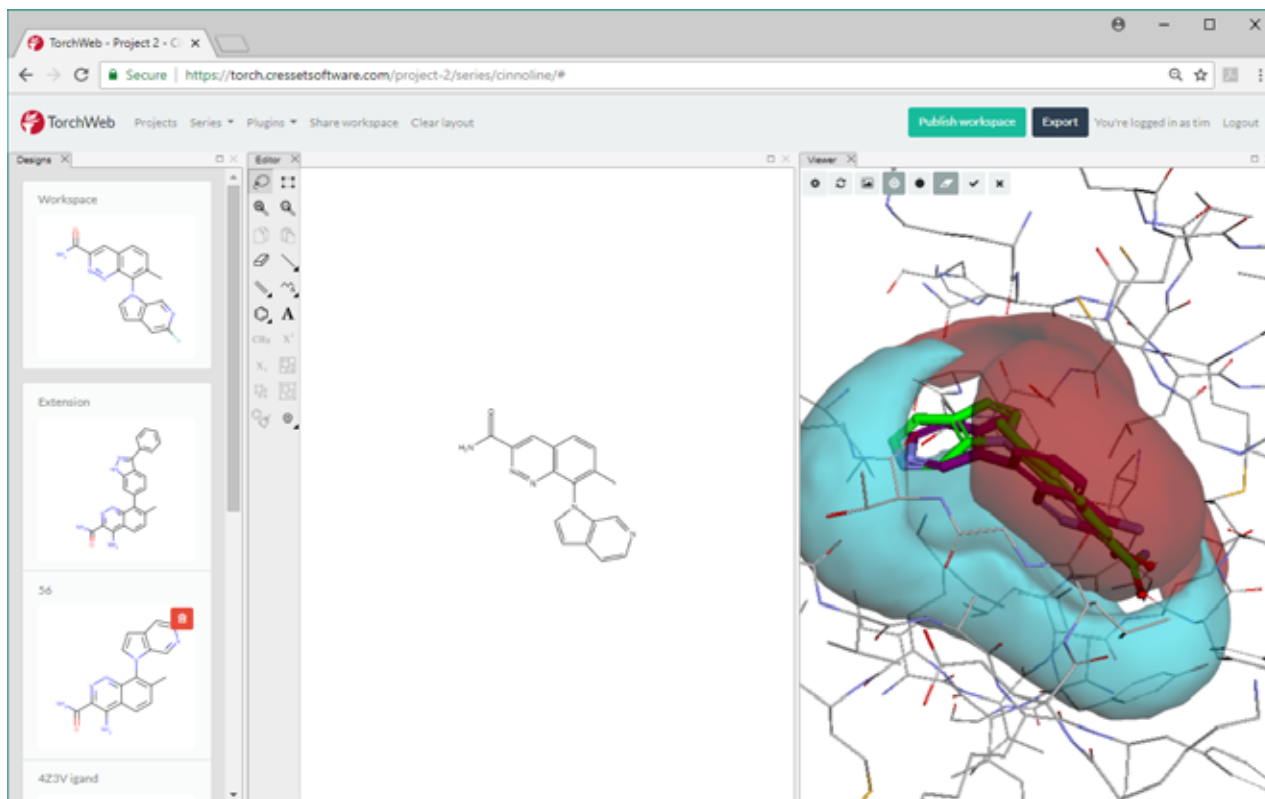
innovative science • intuitive software



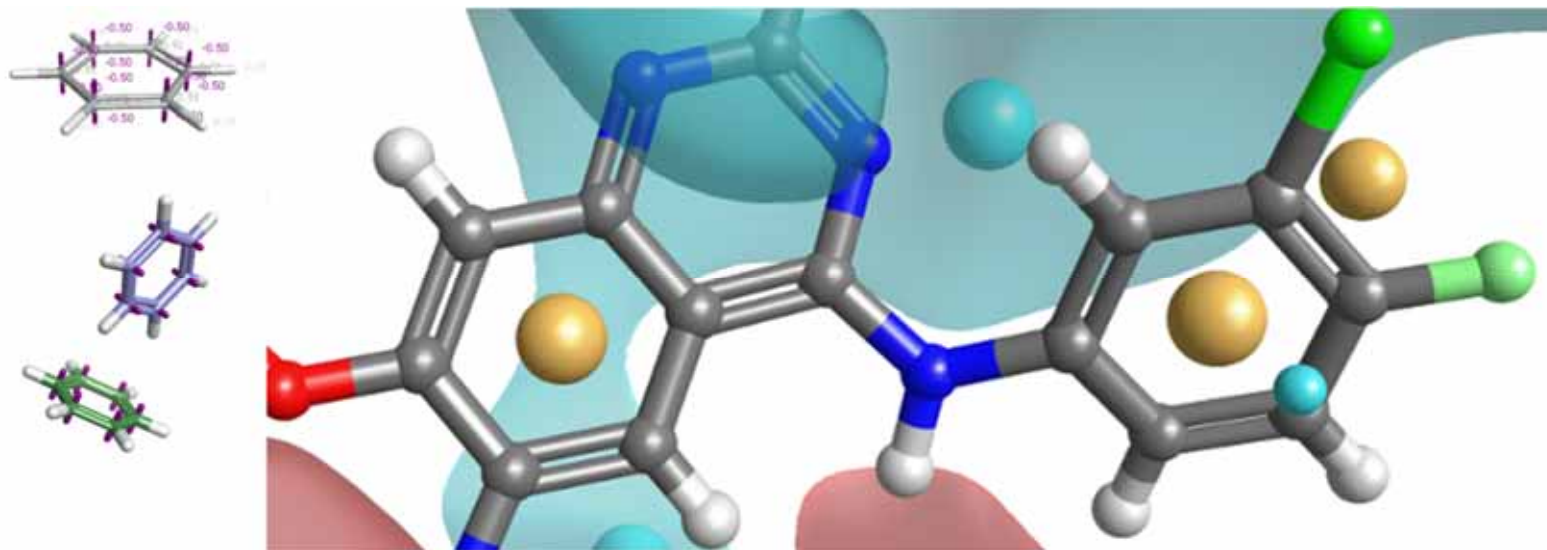
Torx™: Connected Chemistry

The next generation chemistry platform

# Update on 'Project TorchWeb'



# Cresset: The Science



blaze



spark



forge



flare



torch









# Torch™ – Molecule design using ligand alignment

Customer requests:

Can I draw with ChemDraw? 

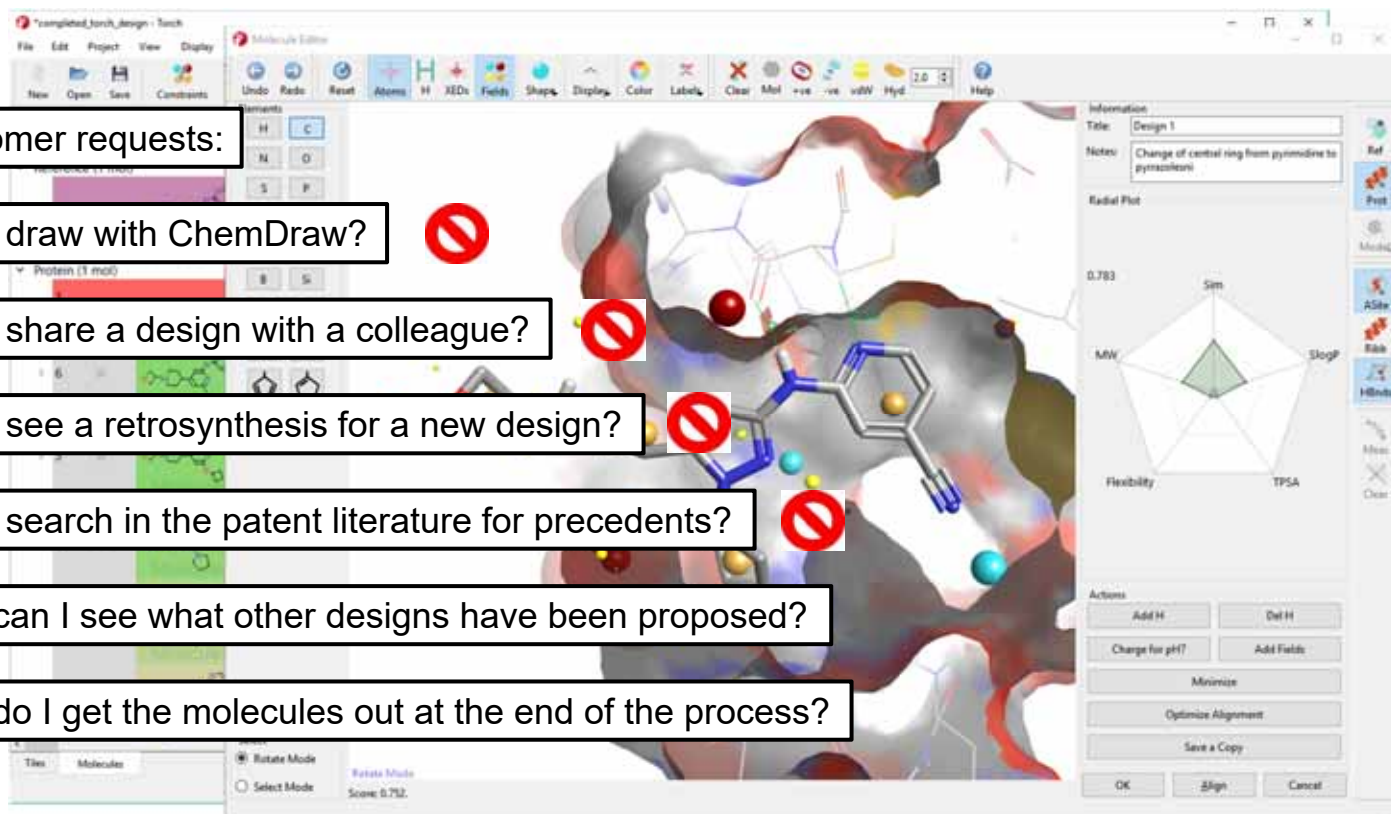
Can I share a design with a colleague? 

Can I see a retrosynthesis for a new design? 

Can I search in the patent literature for precedents? 

How can I see what other designs have been proposed?

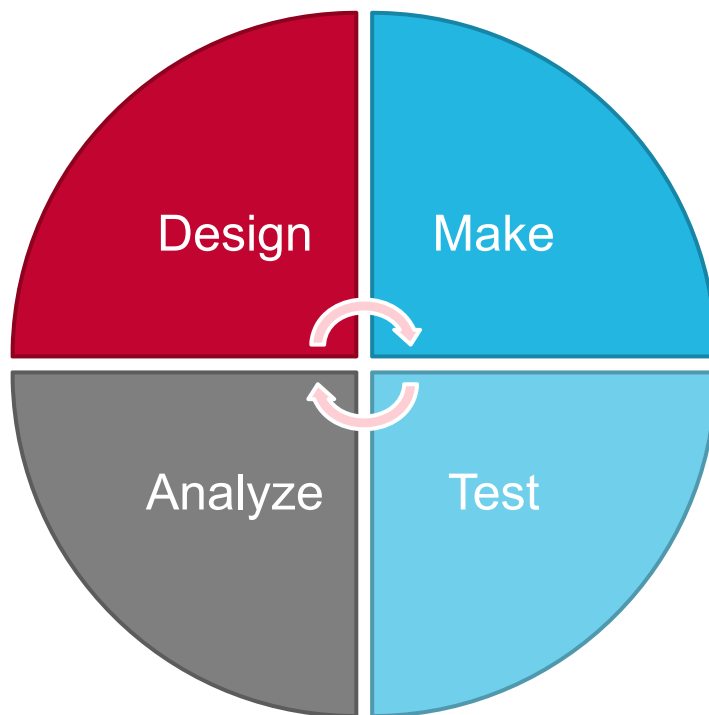
How do I get the molecules out at the end of the process?





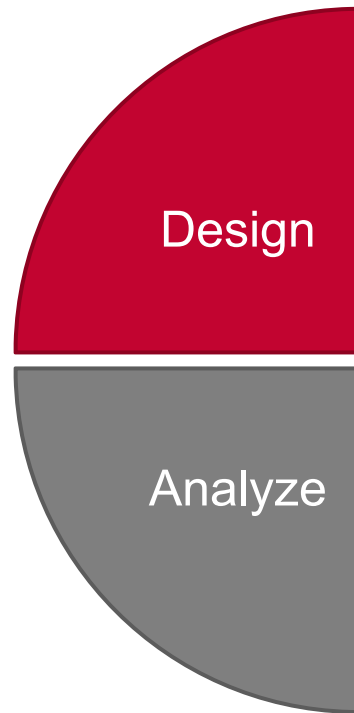
# The molecule discovery cycle & applications

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# Every task has specialist requirements

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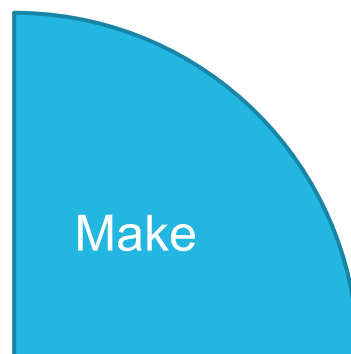


- > **Context**
  - > Protein, prior art, ...
  - > Hypothesis generation
- > **Novelty**
- > **Precedent**
- > **Properties & Predictions**
- > **Redundancy**
- > **Data fluidity**
- > **Flexibility**
  - > 2D – charts, graphs etc
  - > 3D – protein contexts, electrostatic and shape analysis
- > **Hypothesis satisfaction, knowledge advancement**
  - > Inspire new designs

## Every task has specialist requirements – make

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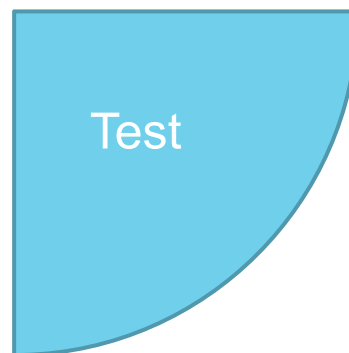
- > Tracking compounds through synthesis
- > Prioritize compounds
- > Resource management
- > Out-source management
  - > Communication
  - > Orchestration
- > Re-prioritization



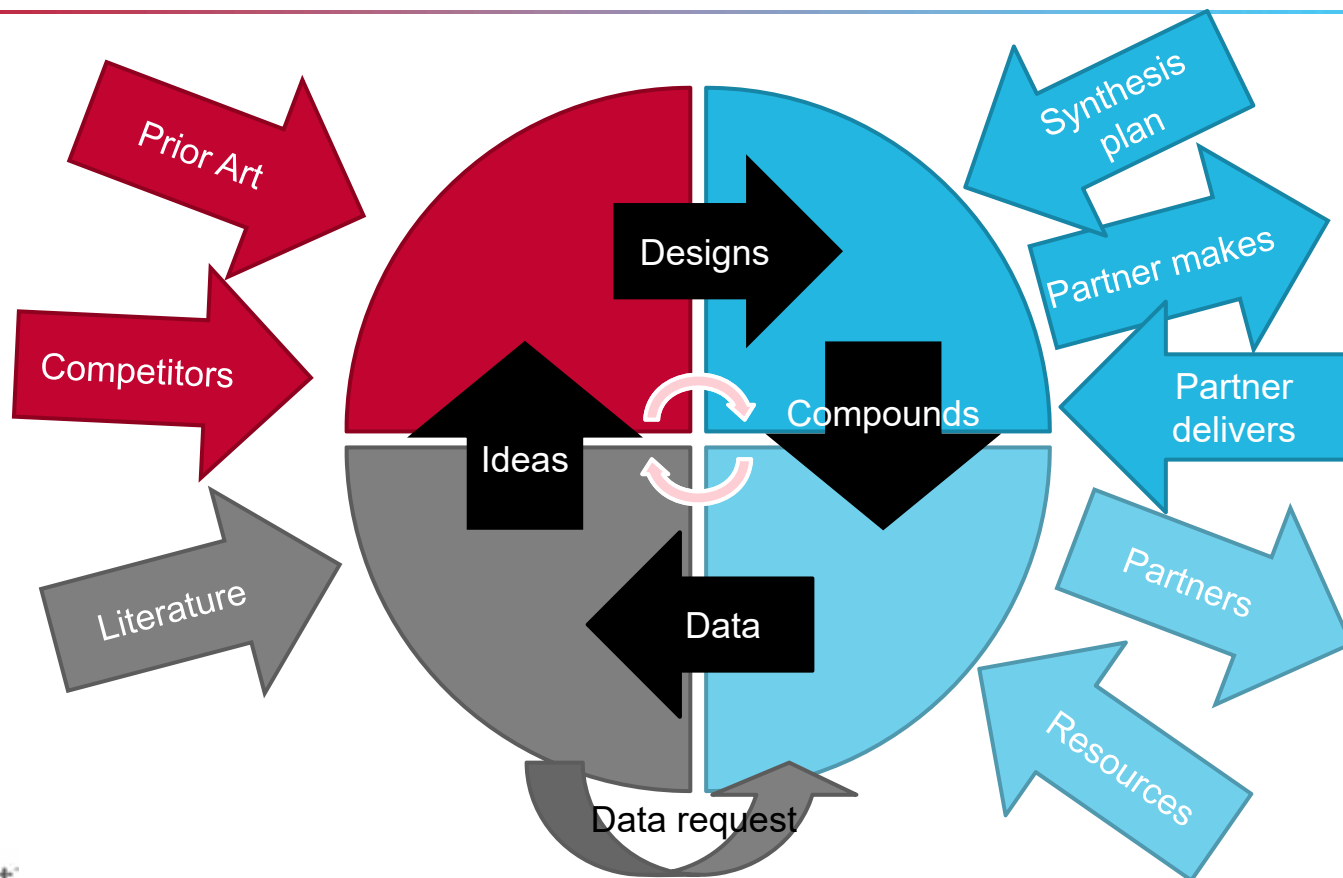
# Every task has specialist requirements – test

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- > A Chemist's view of compounds & assays
  - > Timelines
  - > Capacity
  - > Resources
- > Portal to manage requests



# Information flows in, out and around the cycle



## Information sources increasing and diversifying

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- > Literature
- > Patents
- > Protein-ligand xrays
- > Computer models
  - > AI
  - > QSAR
  - > FEP
- > Computational ideation
- > Public databases
- > Corporate databases
- > Retro-synthetic analysis
- > Reagent ordering
- > CROs
  - > Synthesis
  - > ADME
  - > Panel screening
- > Progress reports
  - > Multiple formats?
  - > Multiple credentials
- > Review meetings
  - > Powerpoint slides
  - > Excel spreadsheets
  - > Email
- > Monthly reports
  - > Individual, project, team, department, ...

# Torx: A central platform for all small molecule discovery chemistry

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- > Web based application
  - > Easy integration of DMTA modules
  - > Integration of 3<sup>rd</sup> party tools (Patent searching, Retrosynthesis, ...)
- > Dedicated applications for each part of the DMTA process
- > Detailed recording of ideas, decisions and contributions
- > Team working as a central theme
  - > Connecting internal and external resources throughout the drug discovery process
- > Modular construction to enable staged uptake and deployment

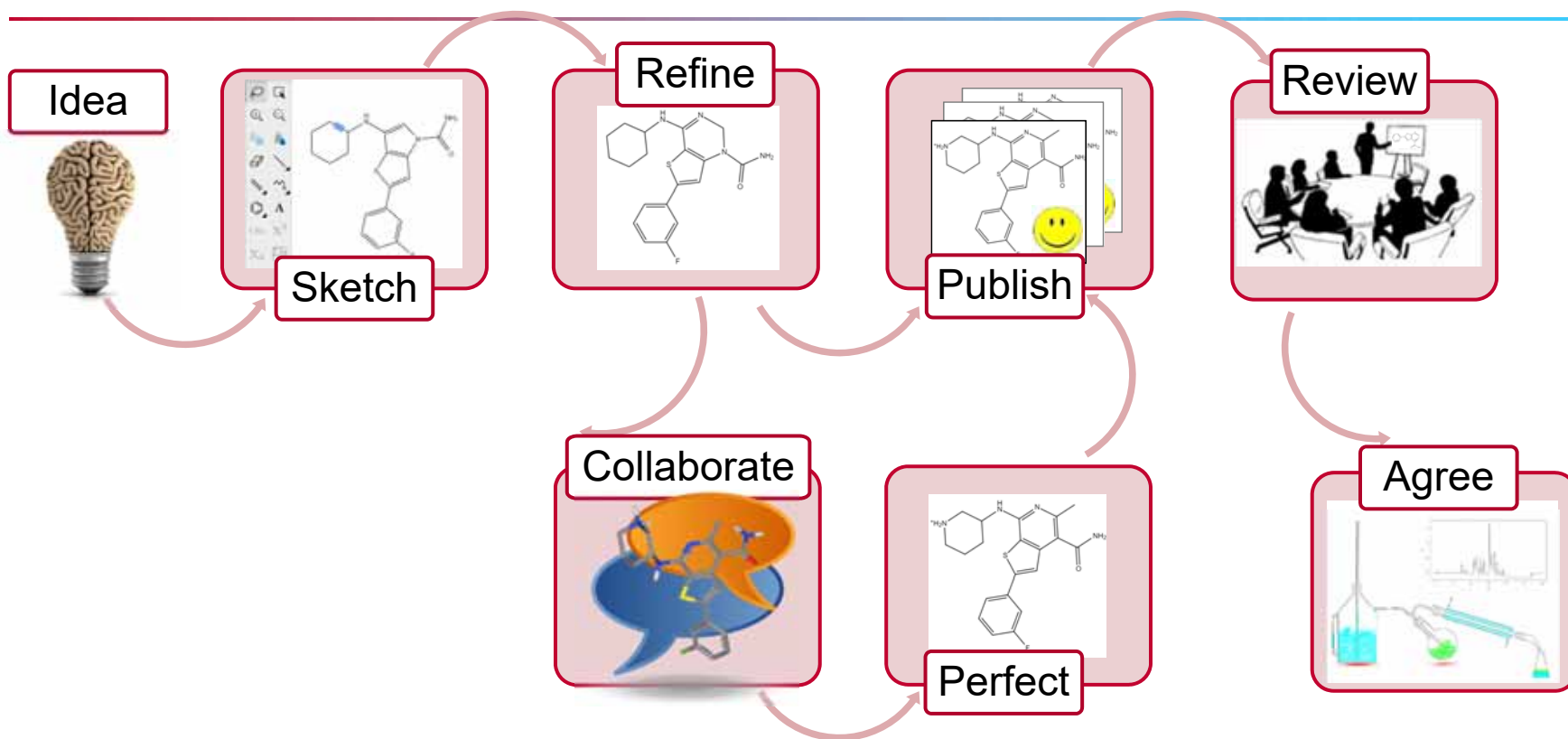
# Torx Design

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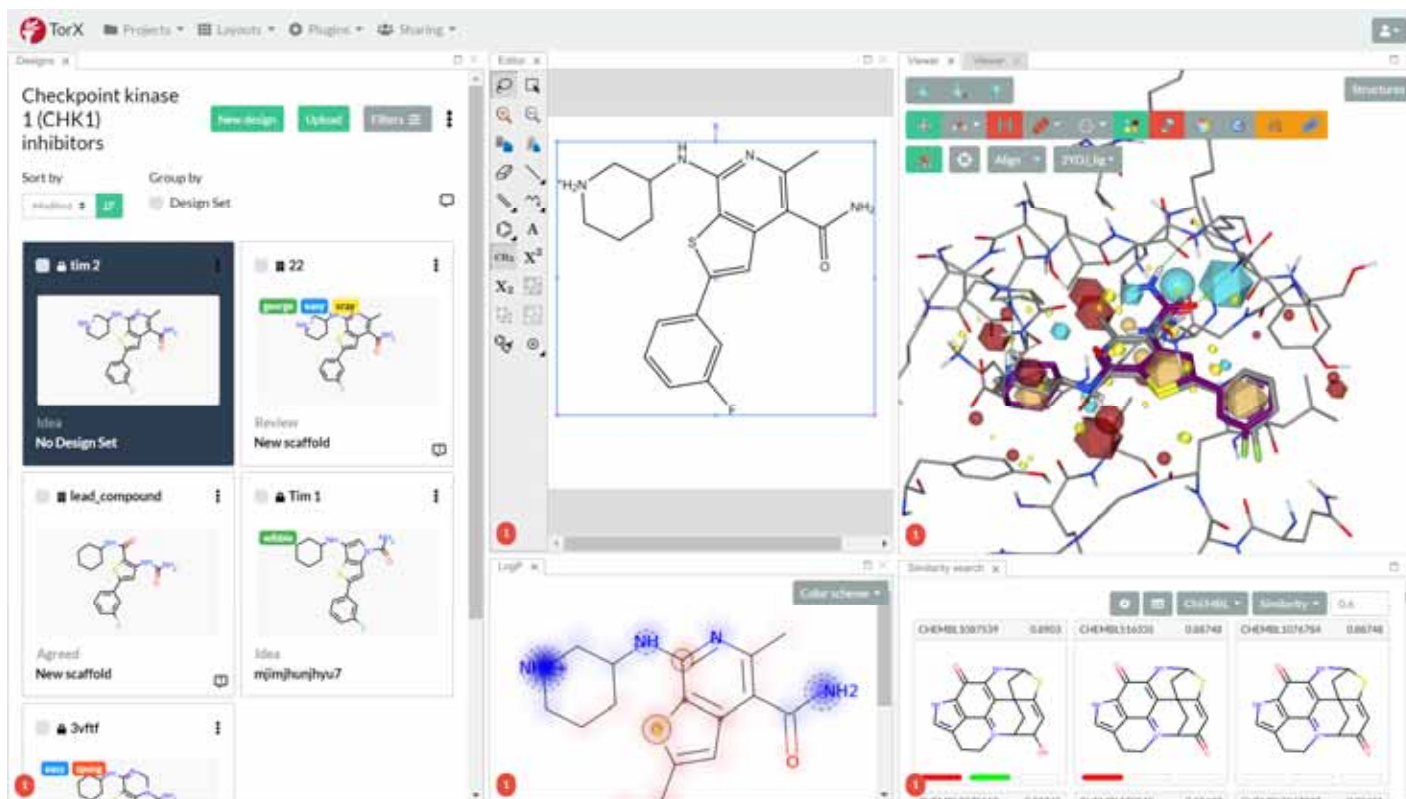
2D and 3D design with all vital information on tap



# Torx design workflow



# Flexible GUI in a web browser



# Flexible information presentation

The screenshot displays the TorX software interface with four distinct plugin views:

- My Designs Plugin:** Located on the left, it shows a list of designs under the heading "Checkpoint kinase 1 (CHK1) inhibitors". It includes a "Sort By" dropdown and a "Group by" dropdown. Below this, there are several design cards, each with a chemical structure and a name like "Tim 2", "lead\_compound", "Tim 1", and "3vtt".
- Editor plugin:** Located in the top middle, it shows a chemical structure being edited. The structure is a complex molecule with a piperidine ring, a pyridine ring, and a benzene ring. A toolbar with various editing tools is visible on the left.
- 3D Viewer plugin:** Located in the top right, it shows a 3D ball-and-stick model of the same chemical structure. The atoms are colored (carbon in grey, oxygen in red, nitrogen in blue). A toolbar with various viewing options is visible at the top.
- Search plugin:** Located in the bottom right, it shows a search results interface. It includes a search bar and a list of results, each with a chemical structure and a name like "CHEBI:330750", "CHEBI:330751", "CHEBI:330752", "CHEBI:330753", "CHEBI:330754", and "CHEBI:330755".

# Design and Review in shared sessions

The screenshot displays the Torx software interface for a shared design and review session. The browser address bar shows the URL: <https://staging.design.torx.cressetsoftware.com>. The interface is divided into several panels:

- Design Panel (Left):** A list of ideas for review, including:
  - Fred: Idea 5,5-bicyclic scaffold
  - tim 2: Idea R-group-1
  - lead\_compo...: Idea 5,6-bicyclic scaffold
  - Tim 1: Review 5,6-bicyclic scaffold
- Editor Panel (Center):** A 2D chemical structure of a bicyclic molecule with a cyclohexane ring, a pyridine ring, and a benzamide group.
- Viewer Panel (Right):** A 3D molecular model of the same structure, showing the spatial arrangement of atoms and bonds.
- Log Panel (Bottom):** A chemical structure with a 'Cofix scheme' and a 'Similarity search' table. The table lists the following data:

Chemical ID	Similarity Score	Chemical ID	Similarity Score
CHEMBL1087539	0.83252	CHEMBL516305	0.82975
		CHEMBL1076704	0.82975

# Design and collaborate in an information rich environment

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## Flexible canvas that holds 'plugins'

- > Cresset developed plugins
  - > 'My Designs'
  - > Design 'Review'
  - > Database 'Search'
  - > 2D 'Editor'
  - > 3D 'Viewer'
  - > Physico-chemical 'Properties'
- > Additional actions
  - > Customizable list of actions from any molecule
- > Custom plugins
  - > SDK with templates for plugin development
  - > Standard templates for web page display, multi-molecule display, picture rendering

## Detailed live sharing of molecules

- > Shared sessions provide team working environment
- > Share molecules not screens – your environment remains unchanged
- > Create a personal view while sharing
- > Permissions on molecules and plugins prevents inadvertent information leakage

## Easy plugin development

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- > Plugins are Vue.js components
  - > See <https://vuejs.org/v2/guide/> for a guide using Vue
- > Development of a new plugin is straightforward
- > We will provide templates and componentry to cover most common use cases
  - > Render an external web page
  - > Image rendering
  - > Tile view of molecules
  - > Etc..

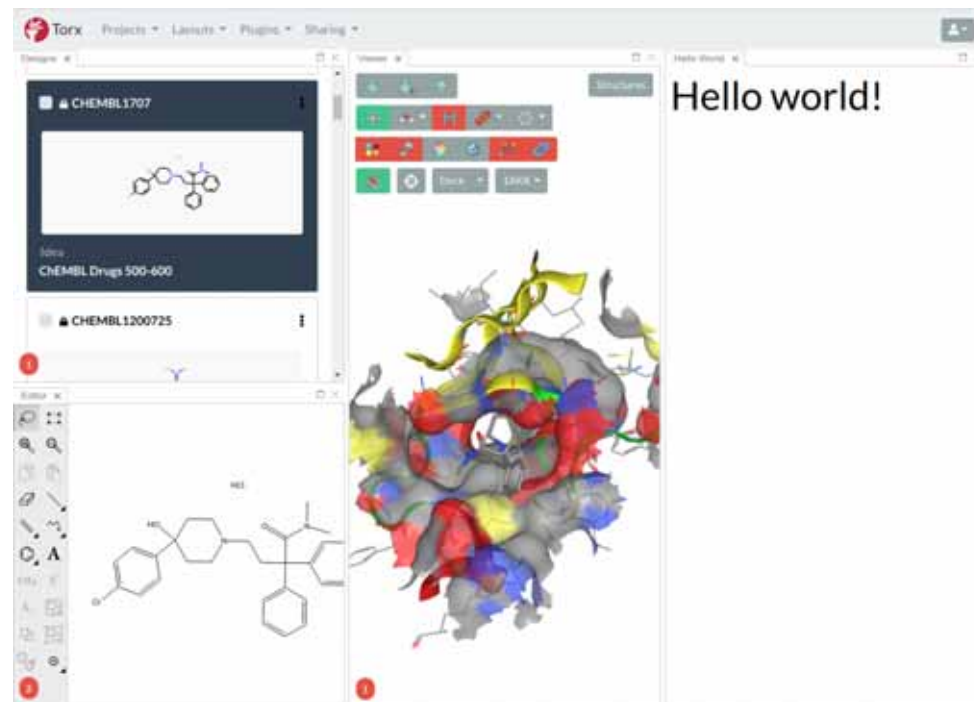
# Torx Plugin Development

```
<template>
  <div class="plugin">
    <h1>Hello world!</h1>
  </div>
</template>

<script type="text/ecmascript-6">
  import Base from '../base/Base.vue'

  export default {
    // Declare that plugin extends the base plugin
    extends: Base
  }
</script>

<style lang="scss" scoped>
.plugin {
  padding: 6px;
}
</style>
```



# Torx Make

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chemTraX



# Design Tracking

The screenshot displays the Cresset DMH DesignSet Tracking interface. The top navigation bar includes the Cresset logo, the title 'DMH DesignSet Tracking', and various controls like 'Row Stacked', 'Column Workflow', and 'Color DesignSet Priority'. Below this, there are buttons for 'DesignSet', 'SSS', 'Filter', 'Export', and 'Alerts'. The main area is a Kanban board with columns for different stages: 'IN DESIGN' (4 tickets), 'AGREED' (1 ticket), 'IN SYNTHESIS' (2 tickets), 'IN TEST' (2 tickets), 'IN ANALYSIS' (2 tickets), and 'COMPLETE' (1 ticket). Each ticket card provides details such as the design set ID, title, lead, number of compounds, and a timeline. For example, the 'AGREED' ticket is '017: 526 Amides with 6-Ar 4-Carboxy-Quinoline' with 88 compounds and a 1-year timeline. The 'IN DESIGN' column contains four 'Torx Design set' labels. The interface also shows a search bar and a user profile 'Tim Cheeseright'.

Designs are tracked on a project process.

They give an overview of the ideas at each stage.

# Synthesis View

The screenshot displays the Cresset software interface for 'DMH Compound Tracking'. The main area is a grid of synthesis assignments. The grid is organized into columns based on the status of the synthesis:

- AGREED:** The first column, with one cell highlighted by a red box. It shows a chemical structure and the name 'Pughman, Pat'.
- IN SYNTHESIS:** The second column, containing several cells with chemical structures and names like 'Pughman, Pat', 'Dessaigne, Tom', and 'Kogutsky, Nadya'.
- SYNTHESIS COMPLETE:** The third column, containing several cells with chemical structures and names like 'Pughman, Pat'.
- SYNTHESIS FAILED:** The fourth column, containing one cell with a chemical structure and the name 'Hartman, Mattie'.
- REGISTERED:** The fifth column, containing several cells with chemical structures and names like 'Pughman, Pat'.

- > Compound tracking provides an overview of all target molecules at each stage of planning & synthesis
- > It gives a visual overview of chemistry assignments for resourcing and prioritization

# Torx Analysis

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# Analysis and design are symbiotic

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## Multi-faceted analysis

- > Data analysis
  - > Chart/Plot driven
- > Binding analysis
  - > 3D derived

## Application to design

- > View key insights at design time
- > Apply insights to new designs
- > Ensure knowledge is gained – avoid learning twice

## Personal & Public

- > Create personal insights
  - > Graph, plot, 3D view, MMP, ...
- > Share with the project team
- > Pick from existing insights

## Flexible data

- > Static & dynamic datasets
- > Use queries to live update
- > Combine & manipulate datasets



# Team working platform

- > Interactive review and design process
- > No more Excel or Powerpoint in meetings
- > Efficient, effective communication with CROs
- > Accessible anytime anywhere

# Improved communications



- > Save time in meetings
  - > More time in the lab
- > Live interactive chemistry tools
- > Faster turnaround times to active chemistry
- > Never miss a decision, never decide blind



## Questions

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