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Customer Case Study

SHY

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- Dr. Theresa Williams, Head of Medicinal Chemistry, SHY Therapeutics

SHY Therapeutics Uses CDD Vault as a "Powerful Resource for Designing New Compounds"

Situation

SHY Therapeutics is building a portfolio of patient-focused programs that meet and surpass standards of care in preclinical models of critically underserved diseases.

SHY's strategy is to focus on the discovery and early clinical stage development of impactful, valuably differentiated therapeutic programs and intellectual property derived from its novel pharmacophore and compound portfolio. The company conducts critical cell-free, in vitro and in vivo experiments in its laboratories on the campus of the New York Medical College, while outsourcing other activities to collaborators including pharmacokinetic studies, compound synthesis, and scale-up.

SHY's drug development strategy leverages the essential roles of ATPases and GTPases by designing small molecules that specifically compete for their interactions with ATP or GTP, respectively, and then modulate their function.

SHY's portfolio includes its lead oncology candidate, SHY-ONC6, an oral inhibitor of the 19S Regulatory Particle of the proteasome (IND filing in second half of 2025), as well as non-covalent pan-KRas inhibitors (clinical candidate designation in second half of 2025) and programs targeting bacterial and fungal pathogens. SHY retains full rights and strong IP for its portfolio.

The company needed a secure central repository to store its small molecules, compounds, and other intellectual property, and to support collaboration between its chemists and biologists.

"We are excited by the number of opportunities we believe SHY has to develop first in class therapeutics to benefit patients with significant unmet medical needs. Borrowing an expression used by competitive rowers, we believe **we have a lot of open water ahead**."

Yaron Hadari & Michael Schmertzler
Founder and Chief Executive Officer & Founder and Executive Chair

Solution

SHY Therapeutics deployed Collaborative Drug Discovery's CDD Vault, the hosted drug discovery informatics platform that securely manages both internal and external biological and chemical data.

SHY Therapeutics uses CDD Vault as its central repository for its novel compound portfolio based on machine learning analyses of traditional and in-silico libraries, proprietary screens and inspired structure activity relationship (SAR) processes. Approximately 24,000 compounds are stored within CDD Vault, which is used as both a foundation for developing small molecule therapeutics and as a target discovery tool.

Benefits

SHY Therapeutics uses a number of CDD Vault benefits, including:

- CDD Vault is "Essential to all of our activity because of the amount of data we generate."
- CDD Vault is a powerful resource for designing new compounds
- CDD Vault provides ease of use
- Enhanced efficiency with saved searches
- Generating bioisosteres with the CDD Vault AI Module
- Seamless access to ChEMBL, SureChEMBL, and Enamine
- Looking ahead to the value of AlphaFold2 and DiffDock
- Protecting intellectual property with CDD Vault
- Finding CDD to be a great company to work with

CDD Vault is "Essential to All of Our Activity Because of the Amount of Data We Generate"

SHY Therapeutics finds CDD Vault central to their operations, from registration to assays and data searches.

"The Vault is essential to all of our activities because of the amount of data we generate," says Dr. Theresa Williams, Head of Medicinal Chemistry at SHY Therapeutics. "To be able to tie data to a specific structure is very important."

Without CDD Vault, the challenge of tracking data can be overwhelming.

"From the number of compounds that we have and the number of assays that are run on each one, trying to organize that and to keep things straight in an Excel sheet would be nearly impossible," Dr. Williams says. "Using the Vault is so efficient, allowing us to pull up a particular structure or set of structures based on a substructure search and then look at the activities that are associated with those structures. The Vault helps organize, for example, the SAR around a particular assay, and to use that to design new compounds."

Dr. Yaron Hadari, Co-founder, CEO & CSO of SHY Therapeutics, agrees.

"With CDD Vault, everything is there," says Dr. Hadari. "First, we register molecules, then we start generating the data, and then we can look at which compounds are the most promising. All those discussions are derived from the data we've saved to our CDD Vault. Sometimes compounds behave in an unpredicted manner and it's easy to identify those, as we screen different assays. We see a compound that behaves as expected, but here's a compound that doesn't. So maybe we need to go back and do another test. Maybe we need to think about another way to find activities. All of this is really easy to do because all of our data is in one place."

CDD Vault is a "Powerful Resource for Designing New Compounds"

SHY Therapeutics finds CDD Vault to be a powerful resource for designing new compounds, including the Vault's precision search capabilities.

"We use the data in the Vault in many ways, including for designing new compounds, where I find it to be extremely powerful," Dr. Williams says. "Specific things, like calculated molecular weight, formula weight, calculating the salt factor, all those things are readily accessible through the Vault. There's a variety of assays in any one project, and you usually are looking for a certain profile that's optimum. There can be trade-offs between assays, and you may lose a bit in one assay, but gain something in another assay. We're not just making laboratory compounds. We want something that's going to therapeutically benefit people. And so we have to have good drug properties as well. All of that data is tracked neatly in our CDD Vault. We can pull out all the data at once and compare one compound versus another. CDD Vault is a powerful resource for designing new compounds."

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> **- Dr. Yaron Hadari, Co-founder, CEO & CSO of SHY Therapeutics**

CDD Vault Provides Ease of Use

SHY Therapeutics was impressed by the ease of use they find in working with CDD Vault, which they administer on their own without requiring a data management specialist.

"Working with CDD Vault is very straight forward," Dr. Williams says. "The ease of use includes the ability to do substructure searches, which give us the ability to look, for example, at the effects of different substituents on a core structure."

SHY Therapeutics researchers use CDD Vault to search on specific assays within a certain range of activities.

"Using CDD Vault we can pull out all the compounds that had a given level of activity in, say, an anti-proliferation assay, and then search for a certain level of activity in a signaling assay," Dr. Williams says. "We can search for all the compounds that have that profile. From there you start to make inferences about new compounds you can design that combine the features."

Enhanced Efficiency with Saved Searches

The ability to create collections of compounds and save search criteria with CDD Vault has proven helpful to SHY Therapeutics.

"We can save collections of compounds so we can just click on the collection, and they all come up," Dr. Williams says. "The ability to save searches is also extremely helpful, in that you don't have to create a new report each time. You can just go to saved searches and reopen assays in a prescribed order, so everything is displayed just as you want it."

Generating Bioisosteres with the CDD Vault AI Module

SHY Therapeutics uses the CDD Vault AI Module, including its AI-powered bioisostere generation.

"The bioisostere generation of the CDD Vault AI Module can definitely spark ideas, as it helps you look at things differently," Dr. Williams says. "I especially like the predictive model with which I can bring in our bioassay data to see what the biological profile of a new compound might look like."

Seamless Access to ChEMBL, SureChEMBL, and Enamine

SHY Therapeutics appreciates the seamless access the CDD Vault AI Module provides for the ChEMBL and SureChEMBL databases, as well as the Enamine catalog.

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- Dr. Theresa Williams, Head of Medicinal Chemistry, SHY Therapeutics

"The ability to access ChEMBL directly from the Vault is helpful when you want to look at a particular compound and see what assays have been tested, the bioactivity, and what target proteins it's hitting," Dr. Williams says. "I think that's very useful."

Dr. Williams sees direct Enamine access from the Vault to be of value especially at the beginning of a project. "At the beginning of our

project we performed high-throughput screening and identified compounds of interest—doing initial SAR by catalog." Williams says. "Back then we ordered it the old-fashioned way. It would have been more streamlined if we could have ordered through the Vault."

Looking Ahead at the Value of AlphaFold2 and DiffDock

SHY Therapeutics values CDD Vault's integration with NVIDIA® NIM™ microservices, including AlphaFold2 and DiffDock. Dr. Williams sees the value in the ability of AlphaFold2 to predict the three-dimensional structure of proteins from their amino acid sequences.

"If you're looking for a drug target binding site, and you generate a structure using AlphaFold, and there are a lot of examples of one particular configuration, you could try to use that to see where might be a good binding site for your compound," Dr. Williams says. "But proteins are flexible, and some can assume an induced conformational fit upon a ligand binding. So there are some risks."

Dr. Hadari also sees potential for using AlphaFold2 in drug discovery—especially for idea generation, while noting that AI can't replace empirical data.

"When you consider small molecule drug discovery and incorporating an AI component, you always need to bring the empirical data," Dr. Hadari says. "AlphaFold can give you a good hint on where to start, and maybe on how to follow up. For example, if you have a small molecule that binds to a specific domain in a protein, AlphaFold can create options for you, but you need to synthesize the compound and make sure it is providing the best binding."

Dr. Williams also sees the value in using DiffDock to predict the three-dimensional structure of a protein-ligand complex and how it will bind to a protein.

"I anticipate DiffDock will be useful especially with known crystal structures when you want to see how well a new compound might dock in a binding site compared to other compounds," Dr. Williams says. "You could also explore how a theoretical compound would bind compared to known compounds."

> ***"Our structures and compounds are our biggest assets. … CDD Vault allows us to share information on an as-needed basis, while protecting our IP."***
> **- Dr. Yaron Hadari, Co-founder, CEO & CSO of SHY Therapeutics**

Protecting Intellectual Property with CDD Vault

Protection of intellectual property is mission critical for all drug discovery companies, including SHY Therapeutics, which values the security of CDD Vault, as well as the ability to use the Vault to grant granular access to IP.

"Our structures and compounds are our biggest assets," Dr. Hadari says. "They are our intellectual property, and what makes us unique."

CDD Vault enables SHY Therapeutics to provide CROs with just the information required to complete tasks.

"CDD Vault allows us to share information on an as-needed basis, while protecting our IP," Dr. Hadari says.

CDD Vault, as a secure repository, also makes it easier to bring together data when filing for a patent.

"In terms of IP, because we're putting all of our data into CDD Vault, when it comes time to write a patent application, we have a ready source for our data," Dr. Williams says.

Collaborative Drug Discovery is a Great Company to Work With

SHY Therapeutics finds CDD to be a great company to work with, in part because of the quality of customer support.

"Whenever I've had a question, the technical team has addressed it promptly," Dr. Williams says. "Sometimes the solution is as simple as an email, other times they might have a video conference to work something out. CDD has very good support and they are quick to respond."

"I think CDD Vault is great, and I think that it's user friendly," Dr. Hadari says. "And whenever we put a note to the technical team, someone immediately gets back to us."

About Collaborative Drug Discovery

Collaborative Drug Discovery provides a modern approach to drug discovery informatics that is trusted globally by thousands of leading researchers. Our CDD Vault is a hosted informatics platform that securely manages both private and external biological and chemical data. It provides core functionality including chemical registration, structure activity relationship, inventory, visualization, and electronic lab notebook capabilities. For more information, visit us at www.collaborativedrug.com.

About SHY Therapeutics

SHY Therapeutics is a private biotechnology company dedicated to advancing small molecule therapeutics that non-covalently target ATPases and GTPases for serious illnesses, including cancer and infectious diseases. ATPases and GTPases are proteins central to the development of many serious diseases. SHY's portfolio of small molecules is designed to target these proteins with high specificity and wide therapeutic windows. For more information, visit SHY Therapeutics at www.shytherapeutics.com and follow the company on LinkedIn.

About NVIDIA

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