



Spotfire Speeds the Discovery Cycle at Infinity

Infinity Pharmaceuticals wanted to increase the quality and speed of its analytical decision making in the discovery of new drug candidates. Spotfire® DecisionSite™ provided the tools to achieve its goals and reduce the crucial “time to next experiment.”

Business Profile

Infinity is a drug discovery company located in Cambridge, MA that focuses on identification of novel anti-cancer compounds.

Application Profile

DecisionSite is used in project teams across the discovery cycle for data access and analysis, compound library design and synthesis, high throughput screening, and focused SAR.

Challenge

- Curating and optimizing data for analysis was difficult due to numerous sources and formats of complex data
- The time to next experiment needed to be optimized to reduce overall discovery process cycle time
- Biologists and chemists lacked an effective common environment for sharing analysis

Solution

- DecisionSite enables easy access of data from multiple sources
- Guided workflows streamline analytical processes
- Intuitive analysis environment leverages both expertise and intuition
- Tight integration with in-house and third-party applications improves efficiency

Results

- Time spent gathering and formatting data was significantly reduced
- Setup time for individual compound retesting was trimmed by days
- Quality of decisions was improved, giving project teams confidence in next discovery steps
- Time to formulate and choose next experiments was reduced by four weeks per year

“With Spotfire, highly visual and interactive data exploration can take place, easily enhancing a scientist’s intuition and expertise in turning molecules into drugs.”

– Dennis Underwood
Vice President of
Computational Sciences
and Discovery Informatics
Infinity Pharmaceuticals

Founded in 2001, Infinity Pharmaceuticals is a drug discovery company that develops novel, small-molecule anti-cancer compounds. Advanced informatics and automation technologies power a product discovery platform based on diversity-oriented synthesis and chemical genetic screening. Infinity’s unique integration of informatics and science has helped to transform its drug discovery cycle to better meet the pharmaceutical industry’s critical need for novel development candidates.

Challenges

Early on, Infinity realized it needed to improve its research informatics architecture to accelerate a drug candidate’s progress along the drug discovery cycle. The cycle begins with compound library design and progresses through chemical analysis, high-throughput screening, hit-picking, and SAR analysis, culminating in focused library development (see *Figure 1*). Problems encountered in the past included difficulty in integrating and visualizing data from many different sources and formats and limited communication between chemists and biologists due the lack of a common analysis environment.

Infinity needed a solution that would help it meet several key criteria:

- Improve the accuracy, consistency and velocity of decision making
- Rapidly adapt to changing end-user workflow and scientific technology requirements
- Allow knowledge to be shared among partners and employees, enabling scientists to focus on science instead of administration
- Access data from multiple sources as well as integrate with in-house and third-party applications.

Solutions

To meet these goals, Infinity selected Spotfire DecisionSite, a highly visual and interactive analytics platform. Over the last three years Infinity has developed numerous Spotfire applications, tightly integrating the software with its own custom code as an integral part of Infinity's architecture. With the help of DecisionSite, Infinity's drug discovery cycle is now fueled by informed, coordinated decision making across chemistry, biology and computational project teams.

"Much of any analysis relies on the expertise and intuition of the chemist and biologist working together, and Spotfire is a great part of this process," says Dennis Underwood, Vice President of Computational Sciences and Discovery Informatics.

Library Design and Development.

The most common entry point into the discovery cycle is the development of virtual chemical libraries. Chemists choose novel, complex scaffolds as the core for a library, and then use DecisionSite together with applications to virtually react potential building blocks with the core's attachment point. Virtual library ideas are analyzed using DecisionSite in order to optimize for various molecular properties, diversity metrics and predictive calculations. Chemists' expertise, experience and intuition, combined with DecisionSite's powerful visual capabilities and the ability to process very large data sets, help to quickly reduce an initial virtual library size of 100-200K compounds down to 10K. A sampling of these compounds is then acquired for testing of synthetic feasibility.

Synthetic and Analytical Chemistry.

In order to assess real properties of the new library, Infinity chemists often create a pilot library that will serve as a property proxy for a potential set. These pilot libraries then go through a formal process of submission, formatting, cleavage, plating, normalization and registration. The scientists assess qualities such as purity, percent yields, physical location, and concentrations, and store the compounds in a LIMS database. Basic visualizations for purity are mapped to workflows of compound managers and are linked to mass spectra and LC trace images. These visualizations are made available for analysis within both DecisionSite and Search, Infinity's custom web search application, allowing chemists to assess purity

over time. Later, scientists in HTS will be able to use these same purity analyses in cases in which assay bias is due to variability in actual sample concentration. Such linking and re-purposing of data across the discovery cycle is one way in which DecisionSite helps to improve the quality of experiment design as well as increase the speed of the experimental process.

Screening and Hit-Picking.

In the next stage, library compounds are delivered to analytical chemists, corporate partners and screening projects. In high-throughput screening, Infinity has configured specific sets of DecisionSite visualizations in a process workflow that allow users to quickly filter results based on activity, experimental controls and background for immediate evaluation of plate Z-factor, while noting artifacts such as edge effects. DecisionSite Guides enable workflows that allow for a structured evaluation process without limiting the analyst's ability to ask and answer ad hoc questions.

DecisionSite Guides facilitate hit-picking processes by linking a series of interactive visualizations to an in-house list management application. Visually marking hits automatically populates the list management system and flags these compounds in a database for plating and retesting. This greatly reduces the time to retest by streamlining the data access, analysis, hit-picking and retest setup and reduces errors in setting up retest experiments.

"With DecisionSite, the time to pick compounds for retest and dose response runs is much faster, and you can be more effective working in a system that's interactive," says Emmanuel Normant, Scientist in HTS/Assay Development and Design.

SAR and Focused Library Development.

With the validated data that emerges from these processes, analysts can use DecisionSite to start evaluating summarized data and generating SAR hypotheses. With DecisionSite they can quickly build queries and launch data, efficiently browsing structures and activities, selecting compounds in a visualization, and retrieving other assay results. DecisionSite automatically builds contextual views from Search that allow the scientists to compare compound properties and multiple assays. The speed and interactive nature of this analysis helps scientists quickly identify the best compounds.



Figure 1: Infinity's drug discovery cycle is a comprehensive, well-informed process across a wide range of expertise.

Results

The integration of DecisionSite with tools such as Infinity Search, curation applications and hit-list management tools has had the effect of shaving up to four weeks per year off of the project team data processing and decision cycles. With DecisionSite, researchers can ask and answer new questions by combining data from multiple sources and interacting with that data in a highly visual intuitive environment to apply their own expertise. At the same time, different functional groups now have a common analytical language and visual environment to make insights based on data generated across the drug discovery cycle. The result is an ability to move more quickly to the next experiment, increasing the probability of finding valuable drug candidates.

"With Spotfire, highly visual and interactive data exploration can take place, easily enhancing a scientist's intuition and expertise in turning molecules into drugs," says Underwood. DecisionSite helps Infinity achieve its "ultimate goal," he adds, which is to "enable users to turn data into information and understanding, allow them to move on to the next experiment, and move Infinity closer to the discovery of a new drug."

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– Dennis Underwood, Vice President of Computational Sciences and Discovery Informatics, Infinity Pharmaceuticals

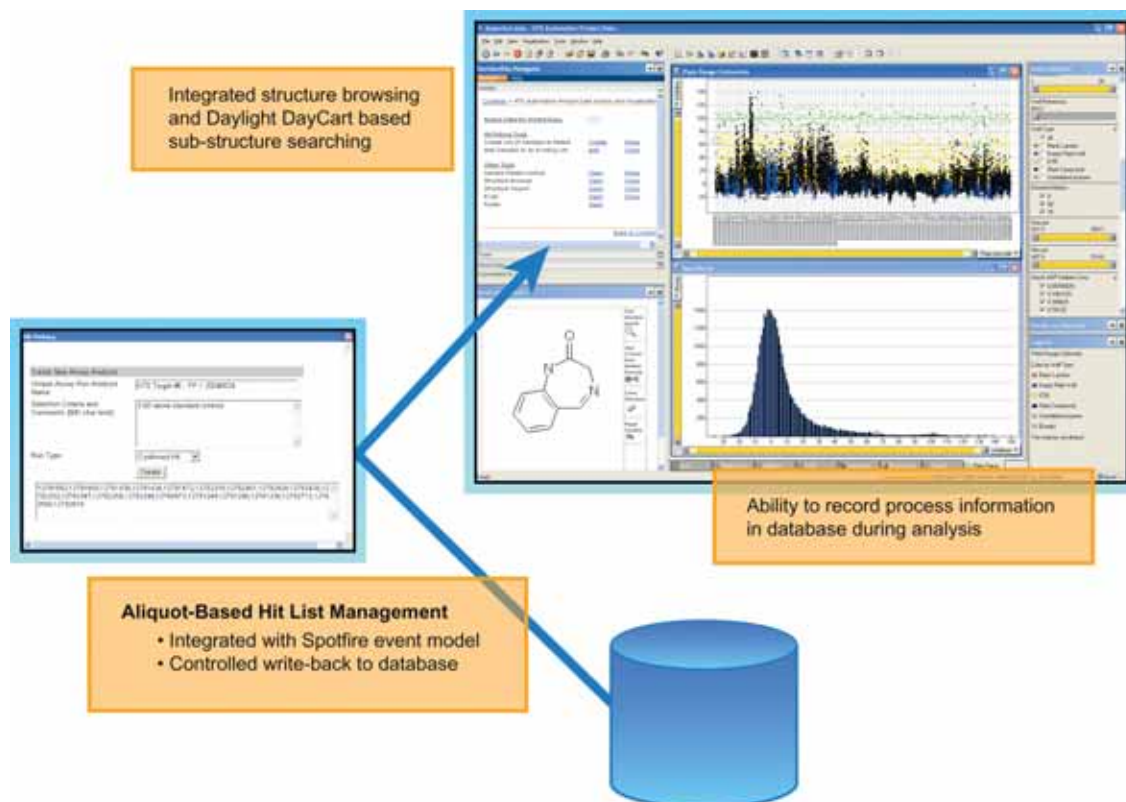


Figure 2: DecisionSite guided workflows link interactive visualizations to a list-management application.

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About Spotfire, Inc.

Spotfire, Inc. provides interactive, visual data analytics applications and services that empower enterprises and their end-users to make fast, accurate business decisions. Over 25,000 users in more than 800 organizations around the world use Spotfire DecisionSite software to analyze their business information in an intuitive, visual environment that speeds analysis and drives confident decision making. The company maintains U.S. headquarters in Somerville, Mass., and European headquarters in Göteborg, Sweden. Additional information can be found at www.spotfire.com.