



Agilent Case Study: Jnana Therapeutics

## Rapid Target Identification in Drug Discovery

With the Agilent RapidFire high-throughput mass spectrometry system, Jnana Therapeutics has streamlined workflows from days to hours.

Jnana Therapeutics, in Boston, Massachusetts, USA, is a clinical-stage biotechnology company who uses their chemoproteomics platform to discover medicines that address challenging disease targets. Jnana is developing therapies for phenylketonuria (PKU) and a broad range of immune-mediated diseases and cancers. PKU is a rare, treatable genetic disorder where the body cannot break down phenylalanine from dietary sources like foods containing protein.

Agilent spoke with Dan van Kalken, Senior Scientist at Jnana Therapeutics, about how he has transformed their analytical approach using the Agilent RapidFire high-throughput mass spectrometry system to accelerate the delivery of drug development candidates.

### Finding a solution

Jnana initially considered purchasing an HPLC with a triple quadrupole mass spectrometer, as this is the standard technique for these types of assays. However, the analysis time of two minutes per sample was too slow to analyze the number of 384-well plates Jnana generates each week.

To meet their throughput requirements, Jnana was forced to outsource their samples to an external lab. The external lab performed the assays on an Agilent RapidFire high-throughput mass spectrometry system. RapidFire provides high-speed sampling and ultrafast automated solid phase extraction, enabling the mass spectrometry data acquisition Jnana requires in only 12 seconds per sample—10 times faster than using traditional LC/MS.



Dan van Kalken

Senior Scientist  
Jnana Therapeutics  
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## Justifying the purchase on a tight budget

With the tight budget of a start-up company, Jnana needed to justify the capital cost of the instrument. “The RapidFire offered the high sample throughput and the data quality we needed and would eliminate the cost of sending our samples to an external lab”, commented Dan. Jnana decided to purchase a RapidFire and bring the assays in-house.

Jnana purchased an Agilent RapidFire, an Agilent 6545 LC/Q-TOF mass spectrometer, and an Agilent 1290 Infinity II LC system. Not only do these instruments support multiple facets of their research program, having them in-house is a boost to their drug discovery program. With built-in robotics and well-plate storage, the RapidFire system can analyze one 384-well plate in as little as 50 minutes. “Running the experiment continuously over a weekend can deliver results for 24,192 individual samples. Having the data for so many samples so quickly meant we were able to decrease the time between new compound generation and the functional assessment of each to a couple of days,” said Dan.

## Instant quadrupling of walkaway time and increased throughput, with accurate results

When Jnana was outsourcing these assays, they used a 96-well plate. With the RapidFire able to hold 64 plates at once, an easy way to quadruple walkaway time and increase throughput was to change to a 384-well plate. Each well plate takes about an hour to analyze. This approach delivers large data sets quickly.

Dan has confirmed the accuracy of the RapidFire assays by comparing the data obtained with that generated by a traditional LC/MS method. He was pleased to find that there is very good correlation between the two data sets, which verified the accuracy of the data from the RapidFire system.

## Tackling additional bottlenecks with RapidFire

With the functional assessment of new compounds reduced to a two-day turnaround, acquiring ADME<sup>1</sup> data for each promising compound became the next bottleneck in Jnana’s workflow. ADME data was taking 2-3 weeks to obtain when outsourced, meaning Jnana’s program wasn’t as efficient as it could be—they couldn’t optimize all the parameters of the molecule within the same iteration of compound design.

Again, Dan turned to RapidFire for a solution. He started to develop RapidFire assays to generate the ADME data in-house, with the microsomal stability assay being first—this assay indicates how likely the drug is to be stable in the body. The assay is traditionally run by HPLC, which takes about two minutes per sample. By moving the assay to the RapidFire, Dan could generate metabolic

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<sup>1</sup> Absorption, distribution, metabolism, and excretion, also known as “ADME,” are the internal processes that describe how a drug moves throughout and is processed by the body—so is an indicator of how well the compound will function as a drug.

stability data within a fraction of the time, compared to industry standard methods. RapidFire can collect data across six time point plates, each with 384 wells consisting of 128 compounds in triplicate, in just 7 hours—only 12 seconds per sample.

“Being able to run microsomal stability assays within the same day as the functional assays really accelerated our drug discovery program—it removed the bottleneck of outsourcing the stability assays,” said Dan. “We just would not have been able to find a development candidate for our PKU program as fast as we did without the RapidFire instrument.”

## Bringing value to the lab

Dan continues to discover new ways to use the RapidFire for a growing list of assays. He has already adapted their microsomal stability workflow for other assays, such as measuring CYP inhibition, with minimal work. The adaptability of the RapidFire means it can be used for other critical high-throughput workflows.

“While the biggest benefit to Jnana was the acceleration of our drug candidates to development and the reduced cost of outsourcing, the RapidFire quickly paid for itself by eliminating contract lab fees, reducing solvent use and disposal, and freeing scientists and other technical staff for more value-added work,” said Dan.

## About Agilent RapidFire

The Agilent RapidFire high-throughput mass spectrometry system consists of a sample cleanup and injection system that interfaces directly with a mass spectrometer. The RapidFire can simultaneously analyze multiple analytes in complex mixtures presented by biological samples, and remove contaminants such as salts, buffers, detergents, proteins, and subcellular material. The throughput of the RapidFire system for label-free, biologically relevant data approaches that of optical technologies.

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**Figure 1.** The Agilent RapidFire high-throughput mass spectrometry system.

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