brightseed

Case Study

"Pharmavite struck a deal with Brightseed to use Forager to help us create a new $100 million (annual sales) sleep supplement brand."

Forbes in speaking with Pharmavite, May 2022

Nature Made

Executive Summary

What | Page 2

The Pharmavite and Brightseed partnership utilized Forager, Brightseed's proprietary natural compound library and A.I. platform, to discover differentiated sleep and stress products with novel and clinically proven solutions.

Why | Page 2

Pharmavite needed scientifically proven and economically viable novel ingredients with industry-disruptor potential. Compared to the industry norm, Brightseed offered a less costly and more efficient novel compound discovery and development process.

How | Page 3

Brightseed and Pharmavite worked together to choose biological targets that could lead to novel supplements that help improve sleep and help reduce feelings of stress. Brightseed used Forager to predict a set of plant compounds that could work within the desired targets, and evaluated the likelihood of success for each target based on computational confidence as well as commercial viability.

Results | Pages 4-7

Forager predicted dozens of new-to-science bioactives from scalable plant sources, with potential for highly differentiated IP protection from a total of >2000 bioactives. Pharmavite chose to continue the partnership into the next phase, which will include validation of the compound predictions via preclinical models. After validation, Pharmavite and Brightseed will have a subset of compounds that can be taken into clinical trials and commercial development.

> *"With Brightseed we saw speed on the science side as well as speed on the commercialization side [compared to traditional development processes]. They allowed us to understand other aspects of the end-product marketability based on the plant sources identified. Knowing how readily available the bioactive compound is in the food supply gave us confidence in our freedom to operate."*
>
> **Tobe Cohen, Pharmavite**
> Chief Growth Officer

“In our industry, it’s hard to differentiate, there are so many commodity ingredients for health. It’s usually a matter of slightly changing the dose or changing the ingredients, but at the end of the day the end products are very similar.”

Susan Mitmesser, Pharmavite
VP, Science & Technology

A case for category disruption

According to the Mayo Clinic sleep related problems affect 50-70 million Americans and according to the American Psychological Society 84% of Americans feel emotions associated with stress, which is why sleep and stress are important health targets for supplement companies. The pandemic has increased US consumer desire for efficacious and scientifically-validated options within these health areas. There is a strategic opportunity for category disruption through commercializing novel plant compounds that impact sleep and stress biological targets in unique ways.

The Pharmavite and Brightseed partnership utilized Forager, Brightseed’s proprietary natural compound library and A.I. platform, to discover differentiated sleep and stress products with novel and clinically proven solutions.

Pharmavite, a subsidiary of pharmaceutical company, Otsuka and manufacturer of Nature Made supplements, shares the belief with Brightseed that solutions to human health issues exist within plants - and that substantial unrealized potential remains in natural sources. Pharmavite needed scientifically proven and economically viable novel ingredients with industry-disruptor potential. Brightseed offered just that solution, with its Forager platform providing a less costly and more efficient novel supplement discovery and development process compared to the industry norm.

Establishing the biological targets for a successful partnership

The Pharmavite discovery program was split into two parts: products for (1) sleep and (2) stress. The sleep program focused on predicting compounds that positively impact sleep onset and maintenance through biological targets within the Orexin system. The stress program sought to predict compounds that positively impact stress and mood through biological targets within the Glutamatergic system. Pharmavite and Brightseed worked closely together to choose these biological targets, based on Pharmavite's needs and by leveraging the expert recommendations from our in-house Translational and Clinical Research team.

Once the biological targets were set, Brightseed utilized Forager to predict a set of potential plant bioactive compounds acting on targeted mechanisms.

Novel discoveries for sleep and stress

The results from the first phase of this partnership demonstrated Forager's ability to uncover the expansive opportunity for novel and natural modulators of sleep and stress.

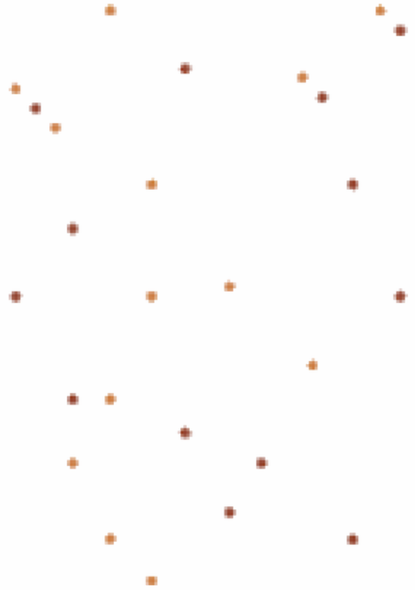
Compound discovery for sleep

For sleep, of the 1521 compounds predicted for potential in vitro validation, OX1R and OX2R modulators within the Orexin system were selected.

These targets were selected because of the strength of evidence among all evaluation criteria, with particular emphasis on safety and efficacy.

For the predicted compounds, there were over 1323 plant associations allowing for higher plant sourcing flexibility and commercial scalability.

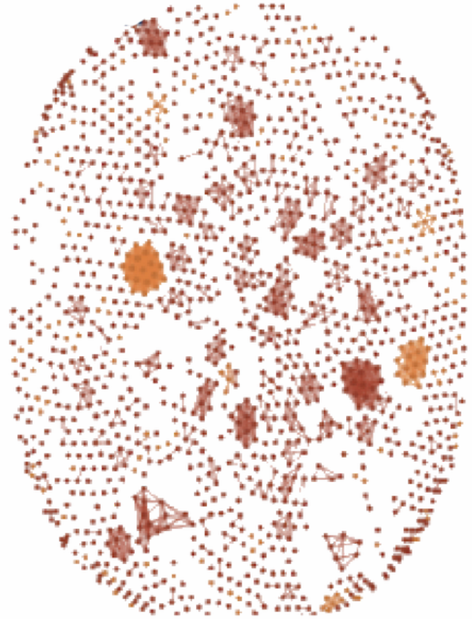
Known to literature



Approximate number of compounds known in public literature as modulators of selected sleep targets.

Forager compound predictions

1521



Compounds for sleep targets

Target 1

Target 2

1521 high-ranking predicted phytonutrient compounds with plant sources & BBB permeability across 2 biological targets.

Compound discovery for stress

Of the 591 potential bioactive compounds predicted for potential in vitro validation, mGlu2 and mGlu3 modulators within the Glutamatergic system were selected.

These targets were selected because of the strength of evidence among all evaluation criteria, with particular emphasis on biological evidence and freedom to operate.

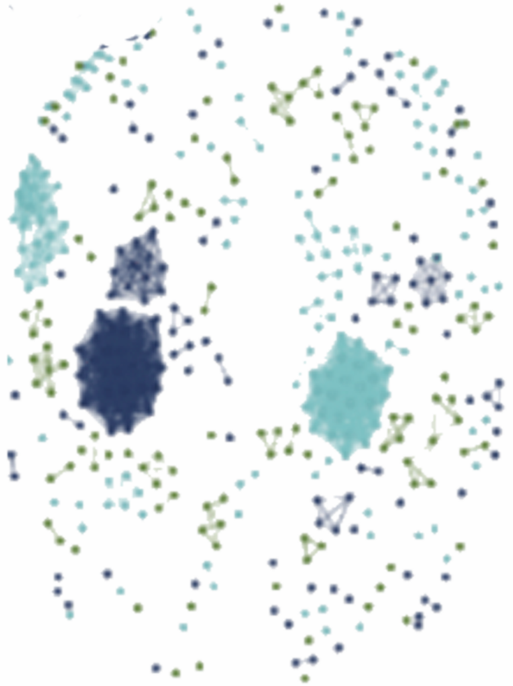
Over 200 plant sources with a history of human use were predicted to contain these compounds allowing for higher plant sourcing flexibility and commercial scalability.

Known to literature

Approximate number of compounds known in public literature as modulators of selected stress targets.

Forager compound predictions

591



Compounds for stress targets

Target 2

Target 3

591 high-ranking predicted phytonutrient compounds with plant sources & BBB permeability across 3 biological targets.

Continuing partnership to validate discoveries and translate them to commercial sales

Following in silico discovery, Pharmavite selected the compounds with the strongest predictions for sleep and stress to continue into in vitro validation. This 12-month process will leverage Brightseed's in-house biology team to design, test, and optimize specialized bioassays to assess the biological activity of the predicted bioactive compounds.

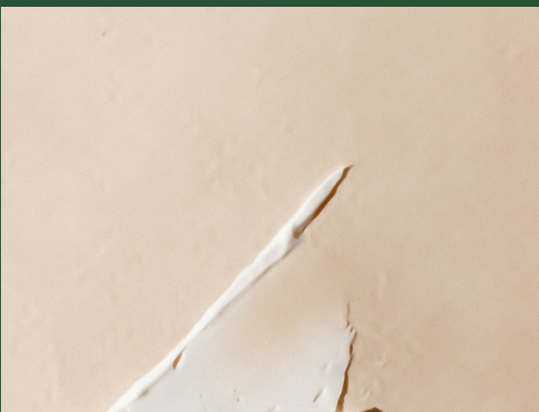
At the conclusion of the in vitro validation phase, Pharmavite and Brightseed will possess a subset of compounds with in vitro confirmed bioactivity that will undergo safety, efficacy, intellectual property, and regulatory review to maximize the likelihood of subsequent clinical and commercial success.

The Brightseed discovery process takes only 4-5 years to yield commercial products, which is half the time of a traditional discovery to product commercialization timeline.

Immediately after in vitro validation, Brightseed protects discovered compounds by securing patents in a wide variety of categories including Application & Use, Whole Food Enriched Product, Extract Composition, Composition of Matter, and Process & Enrichment. Brightseed has a history of securing patents for their own commercial sales - they currently possess 2 issued patents and 6 pending patent families.

Innovate naturally with Brightseed

Brightseed partners with innovation leaders across a range of industries to discover, validate, and bring to market natural bioactive solutions for health. Our A.I. platform, Forager, provides differentiated health insights and uncovers IP-protected bioactives that impact critical areas of human biology.



The world's most expansive library of plant compounds

Brightseed's Forager has already mapped over 2 million natural compounds, 20x what the world knows. Forager uses A.I. to connect plant data with biological models to unlock answers for consumer needs.

20x

more plant compounds than previously known to academia and industry.

Using Forager, Brightseed identifies what's in a plant, and determines health benefit implications through a curated model of human health.

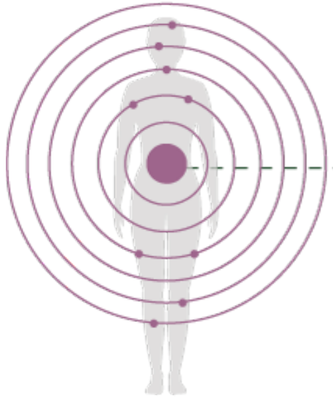
Further capabilities include clinically validating predictions through our in-house biology team and identifying the most viable compounds for commercialization through an ever-growing index of plant sources. Brightseed's platform is constantly updated using diverse plants and tissue types with a history of human use, greatly increasing the chance of translational success.

Brightseed's natural compound discovery

Brightseed's discovery process starts with in silico prediction. Our A.I., Forager, computationally predicts bioactive compounds that are likely to interact with the chosen biological targets in specific ways (e.g., inhibition or activation). Brightseed then ranks the predicted compounds based on four criteria: biological evidence, bioactivity & plant predictions, computational confidence, and freedom to operate. Based on this evaluation, compounds are chosen for the next step of in vitro validation, which uses bio-assays to assess whether the compound(s) have the predicted bioactivity.

Discovery Phase 1A:
AI Predictions

Discovery Phase 1B:
Validation



Identify the health benefit and underlying biological target

Predictions of all plant bioactives

Plant source identification and selection

Lead compounds are identified and whole plants are fractioned

Individual compounds/ whole pant fractions are validated for in vitro efficacy

A platform for discovery with unparalleled speed and precision

Brightseed's in silico predictions and preclinical validation models provide time and cost savings compared to existing "trial and error" processes in ingredient development.

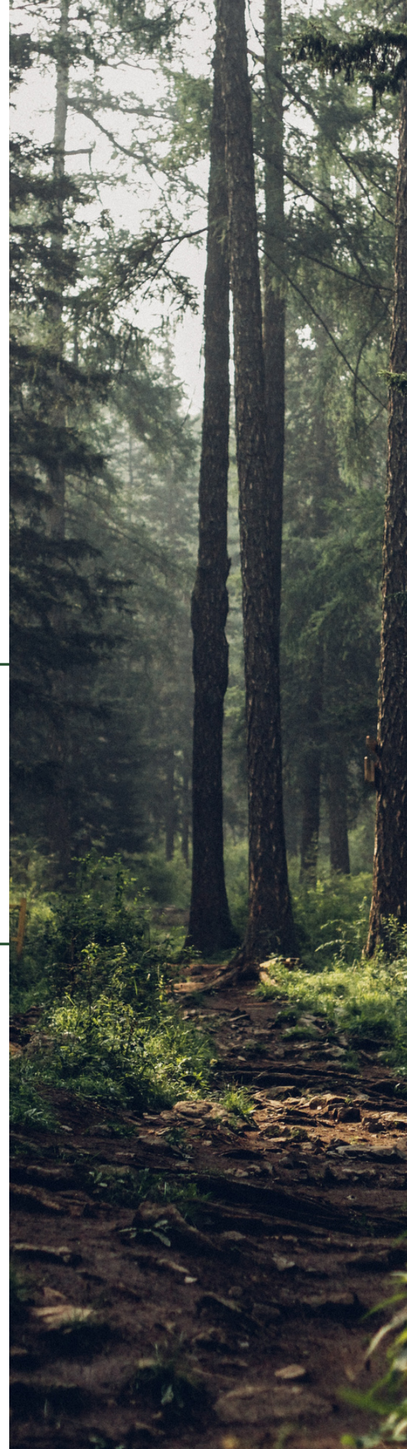
This is the result of Forager's accelerated identification of bioactive compounds and unique ability to connect those compounds with pathways in human biology to identify potential health benefits.

Where traditional high-throughput screening typically produces hit rates between 0.01 - 0.14% (1) at a cost of $0.10 to $1.00 per tested sample (2), we have a track record of delivering hit rates >10x higher with substantially reduced costs.

100x Higher hit rate than traditional pharma

20x More coverage of plant compounds than known before

10x Faster discovery than high-throughput screening



Proven performance: better solutions, faster

This table shows hit rate percentages from Brightseed's internal discovery pipeline, across a number of health targets, compared to conventional discovery program benchmarks within the same health targets.

	Benchmark	Metabolic Health Discovery	Sugar Management 1st Discovery	Sugar Management 2nd Discovery	Sugar Management 3rd Discovery	Cognitive 1st Discovery	Cognitive 2nd Discovery
Health benefit	NIH-funded high-throughput medicinal chemistry[1-4]	Helps body process unhealthy fat	Improves body's intake and response to sugar			Improves ability to fall asleep	
Leads	1	3	2	2	5	1	2
Hit rate	0.03%	4%	7%	9%	17%	17%	34%
Effectiveness	1X	1 - 15X	TBD	TBD	100x	TBD	TBD
Time to discovery	3 years	3 months	4 months	4 months	8 months (includes novel assay development}	2 months	2 months

Direct comparison →

Note: Each Discovery represents a single biological target

brightseed

Citations

1. Zhu, Tian, et al. “Hit Identification and Optimization in Virtual Screening: Practical Recommendations Based on a Critical Literature Analysis.” Journal of Medicinal Chemistry, vol. 56, no. 17, 2013, pp. 6560–6572.,
2. https://doi.org/10.1021/jm301916b.\“Services, Equipment & Pricing.” UWCCC Research, https://cancer.wisc.edu/research/resources/ddc/smsf/equipment-services/.

Contact

info@brightseedbio.com
brightseedbio.com