



Case Study

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

Forbes in speaking with Pharmavite, May 2022



Executive Summary

What | Page 2

The Pharmavite and Brightseed partnership utilized Brightseed's proprietary natural compound library and A.I.-powered platform, Forager, to discover differentiated products targeting sleep and stress. The end-goal of the work with Brightseed is to develop a natural dual Orexin receptor bioactive to deliver sleep benefits and a natural dual mGluR receptor bioactive to deliver stress benefits.

Why | Page 2

Pharmavite's growth strategy identified a need for scientifically proven and economically viable bioactive ingredients with industry-disruptor potential. Brightseed offered a compelling economic and efficient bioactives discovery and development solution to help Pharmavite achieve their business goals.

How | Page 3

Brightseed and Pharmavite collaboratively selected biological targets with strong potential for differentiated bioactive ingredients to help improve sleep and stress. Leveraging the predictive power of Forager A.I., Brightseed highlighted top compound candidates associated with the desired targets based on predicted biological and commercial viability.

Thousands of fractions from hundreds plant species were then screened for top hits through in vitro evidence of their ability to modulate the chosen receptors to positively impact the respective sleep or stress health areas. The top hits in both programs demonstrated strong and promising bioactivity, consistently matching or outperforming positive control compounds.

Results | Pages 4-7

Brightseed found 11 high efficacy candidates for improving sleep and 16 high efficacy candidates for improving stress. Through in vitro validation Brightseed identified the top fractions for each program that showed strong and consistent activity for each benefit area. Pharmavite and Brightseed will now be taking the top hits for sleep and stress into the development phase by first conducting further characterization and isolation of lead fractions, testing for preclinical efficacy in cutting edge rodent models, and then formulating bioactive ingredient prototypes.

“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



A case for category disruption

The Mayo Clinic found sleep related problems to affect 50-70 million Americans and the American Psychological Society reported that 84% of Americans feel emotions associated with stress thereby highlighting the importance of sleep and stress as important health targets for supplement companies. The increased US consumer desire for efficacious and scientifically-validated natural options within these health areas resulting from the pandemic presents a strategic opportunity for category disruption through commercializing novel plant compounds that impact sleep and stress in unique ways.

The Pharmavite and Brightseed partnership utilized Forager, Brightseed's proprietary natural compound library and A.I.-powered 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 bioactive ingredients with industry-disruptor potential. Brightseed offered just that solution, with its Forager platform providing a more cost-effective and efficient bioactive discovery and development process than the industry norm.

Establishing and validating the biological targets for a successful partnership

The Pharmavite discovery program was split into sleep and stress components. Pharmavite and Brightseed worked closely together to select biological targets based on Pharmavite's needs, leveraging the expert recommendations from our in-house Translational and Clinical Research team. The sleep program landed on predicting compounds that positively impact sleep onset and maintenance through biological targets within the Orexin system. The stress program selected biological targets within the Glutamatergic system to predict compounds that positively impact stress and mood. Brightseed then utilized Forager to predict a set of potential bioactive plant compounds acting on targeted mechanisms and provided further evidence through in vitro validation.



Novel discoveries for sleep and stress

The results from the first phase of this partnership demonstrated Forager's ability to quickly uncover the expansive opportunity for novel and natural modulators of sleep and stress, based on in vitro validation.



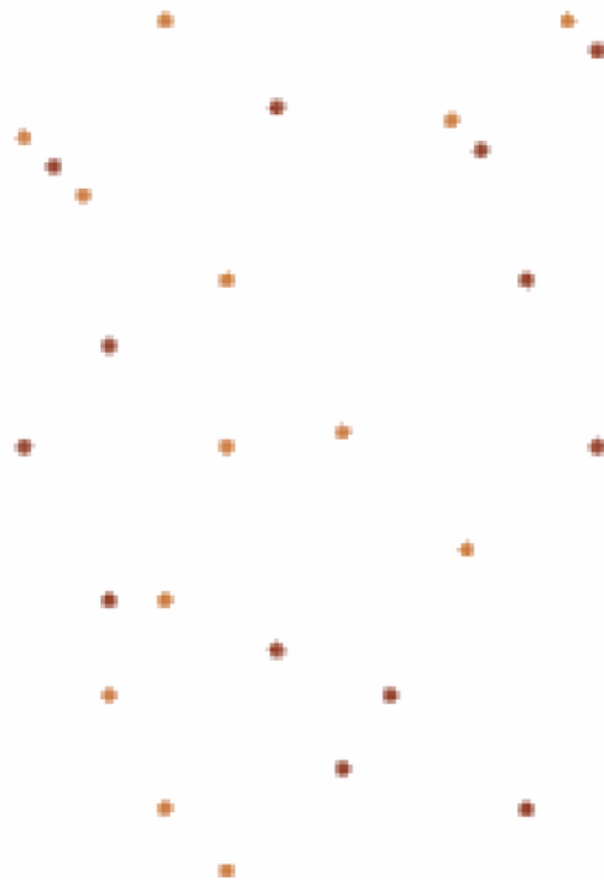
Compound Discovery for Sleep

To deliver sleep benefits, the goal was to develop a natural dual Orexin receptor antagonist. To this end, Brightseed screened 1008 fractions and extracts from 84 plants from the Forager prediction output and found 10 high efficacy candidates for improving sleep. Through in vitro validation, Brightseed identified 4 top fractions and 11 total hits that showed strong and consistent activity for positively affecting sleep by modulating Orexin using a 3 step process:

- In-house optimization of sleep bioassays to screen fractions and samples for dual receptor activity (primary screening)
- Activity confirmation utilizing secondary assays of downstream effectors
- Suitability confirmation for further development by in vitro toxicity and viability testing

To ensure reproducibility each plant was tested from four different plant sources, each in quadruplicate, and top plant fractions consistently ranked higher than positive controls.

Known
to literature



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

*Forager compound
predictions*

1521



Total compounds
predicted for sleep
targets

Target 1 ●
Target 2 ●

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

Compound Discovery for Stress

To deliver stress benefits, the goal is to develop a natural mGluR2/3 antagonist. From the top predicted compounds and plant sources by Forager, Brightseed screened 984 samples from 84 plants, and identified 16 high efficacy candidates for improving stress. Through in vitro validation Brightseed identified 16 top fractions that showed strong and consistent activity for positively affecting sleep by modulating mGluR2/3 using a 3 step process:

- In-house optimization bioassays to screen fractions and extracts (primary screening)
- Activity confirmation in secondary assays of downstream effectors
- Suitability confirmation for further development by in vitro toxicity and viability testing

To ensure reproducibility each plant was tested from four different plant sources, each in quadruplicate, and top plant fractions consistently ranked higher than positive controls.

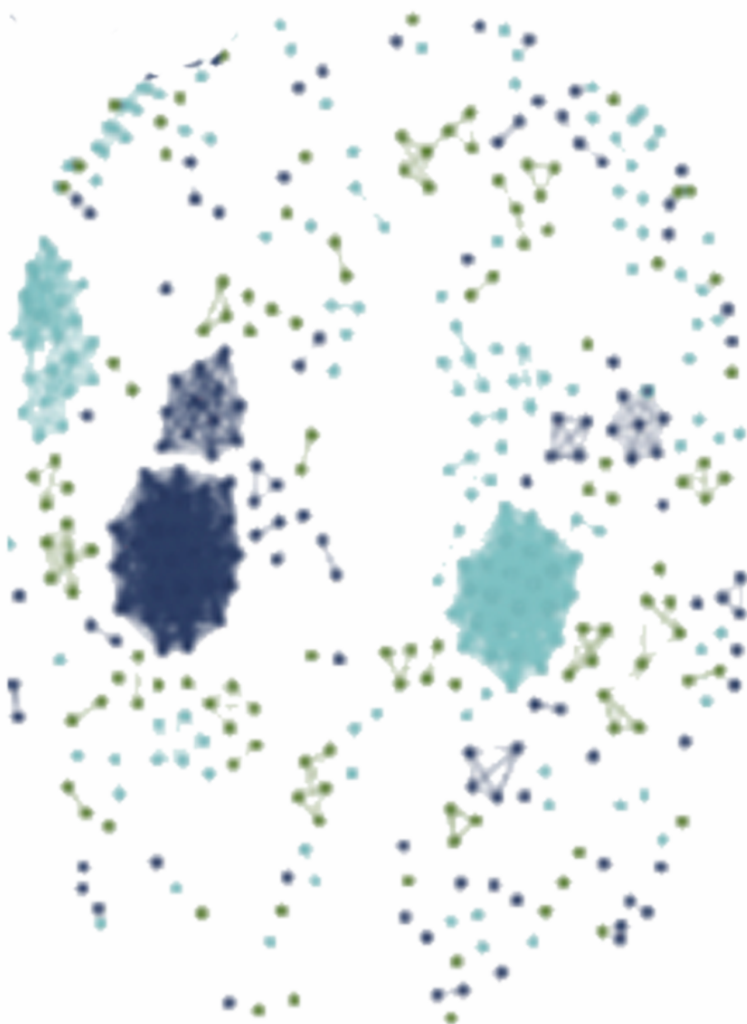
Known
to literature



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

*Forager compound
predictions*

591



Total compounds
predicted for stress
targets

Target 2 ●
Target 3 ●

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

Continuing partnership to validate discoveries and translate them into commercial sales

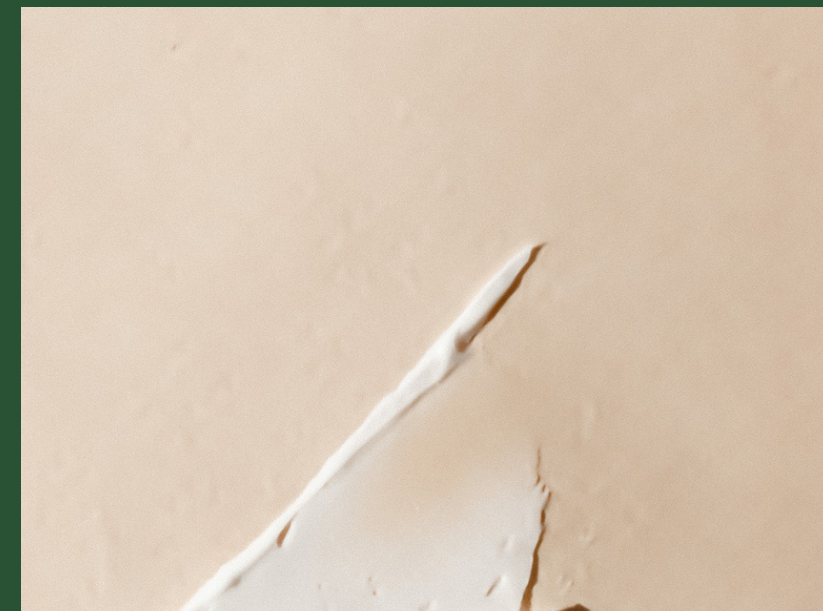
Pharmavite and Brightseed will now be taking selected top hits into the development phase by first conducting further characterization and isolation of lead fractions, testing for preclinical efficacy in cutting edge rodent models, and then formulating bioactive ingredient prototypes.

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 and 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 bioactives from nature for health. Our A.I. platform, Forager, provides differentiated health insights and uncovers IP-protected bioactives that impact critical areas of human biology.



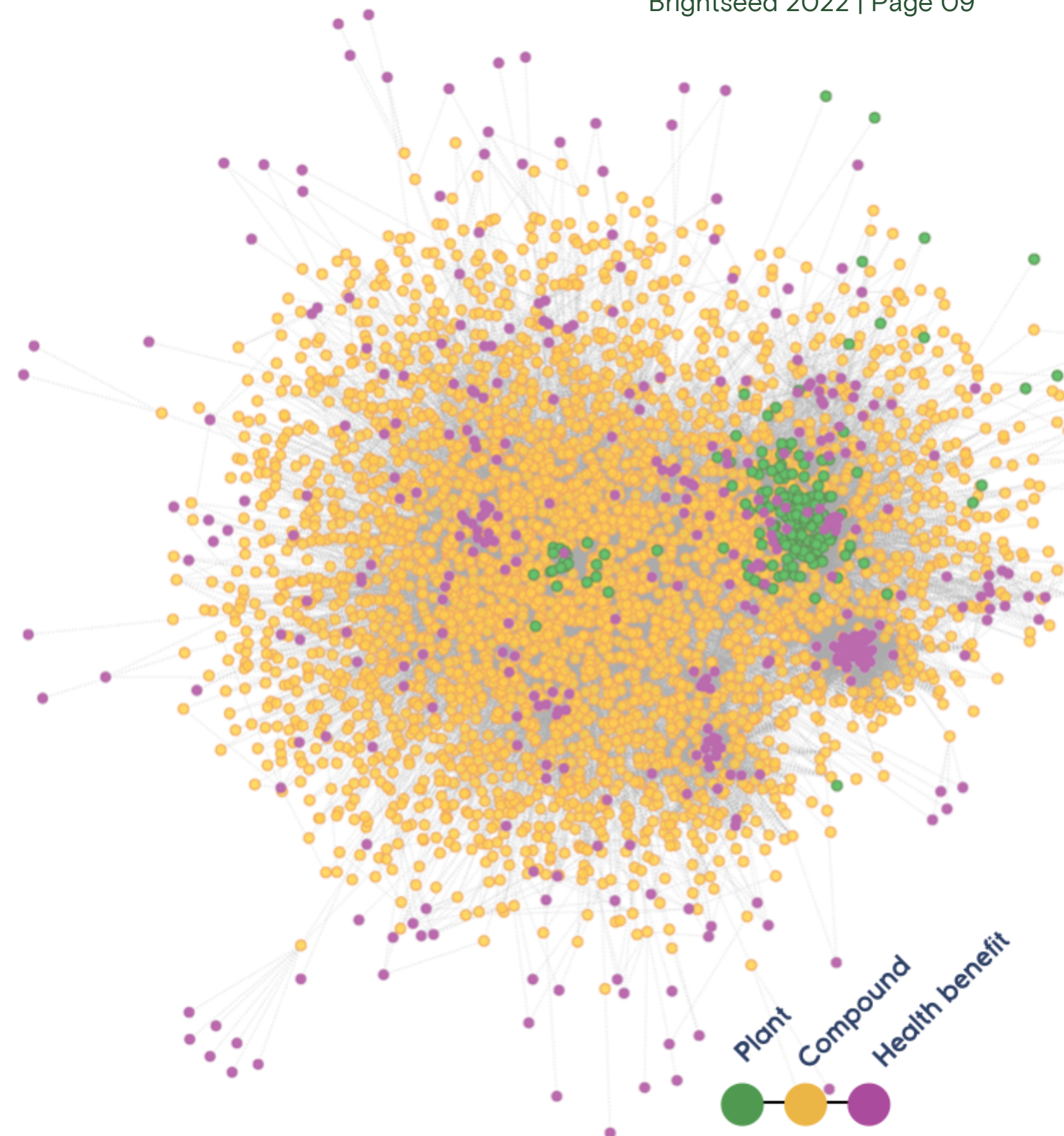
The World's Most Expansive Library of Plant Compounds

Brightseed's Forager has already mapped over 4 million natural compounds, and identified 30K predicated bioactives, targeting 18 health territories. Forager uses A.I. to connect plant data with biological models to unlock answers for consumer needs.

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.

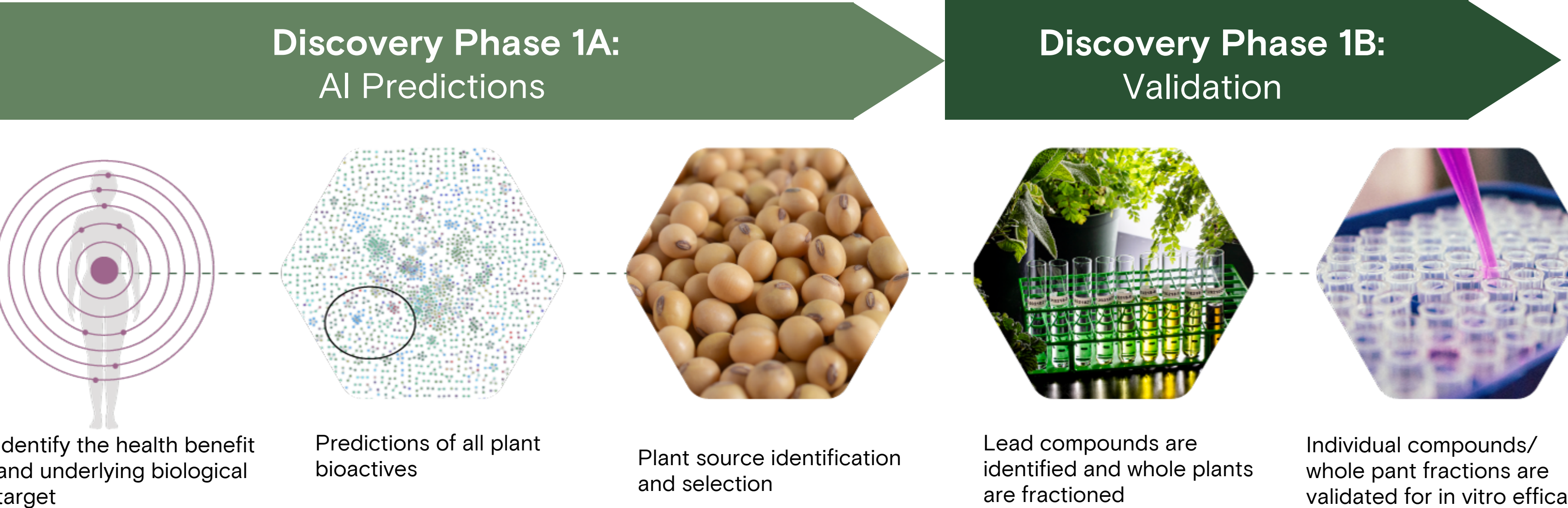
40x

more plant compounds than has previously been documented in published literature.



Brightseed's natural compound discovery process

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. Brightseed also has the in-house capabilities to take the compound(s) through pre-clinical and clinical trials, as well as ingredient development and commercialization.



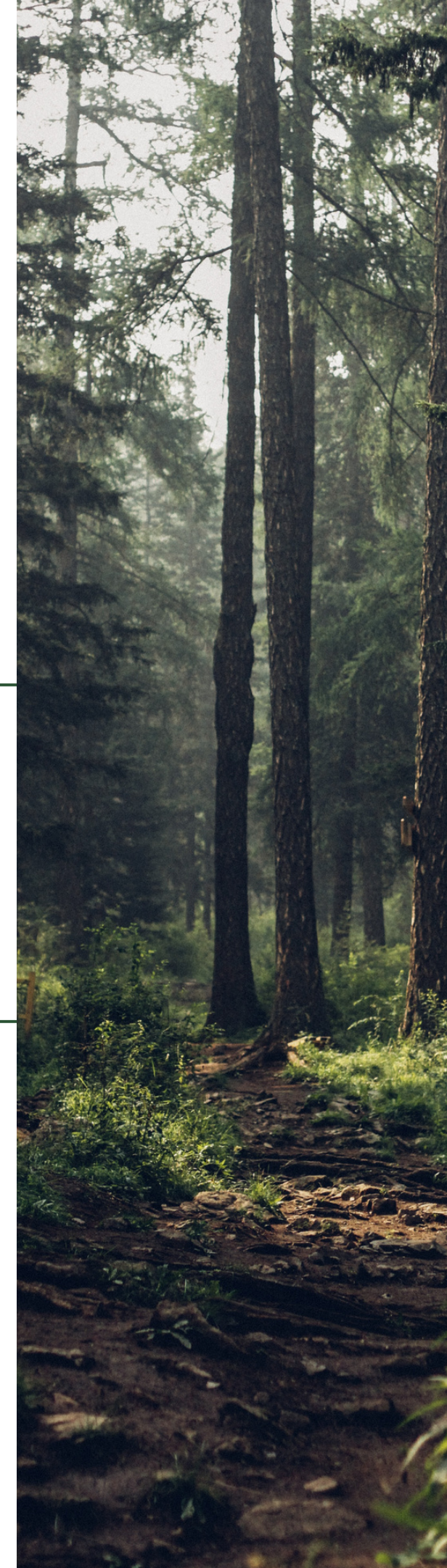
A platform for discovery with unparalleled speed and precision

Brightseed combines A.I. with world class bioactive discovery capabilities to deliver clinically-proven structure function claims and IP-protected bioactive ingredients derived from natural sources. By cutting out the “trial and error” process, development capital can be focused on only those sources with the highest potential biological impact, thereby streamlining innovation and accelerating time-to-market for truly novel and differentiated natural health products.

100x Higher hit rate than traditional methods

40x More coverage of plant compounds than known before

10x Faster discovery than high-throughput screening





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., <https://doi.org/10.1021/jm301916b>.
2. "Services, Equipment & Pricing." UWCCC Research, <https://cancer.wisc.edu/research/resources/ddc/smsf/equipment-services/>.

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