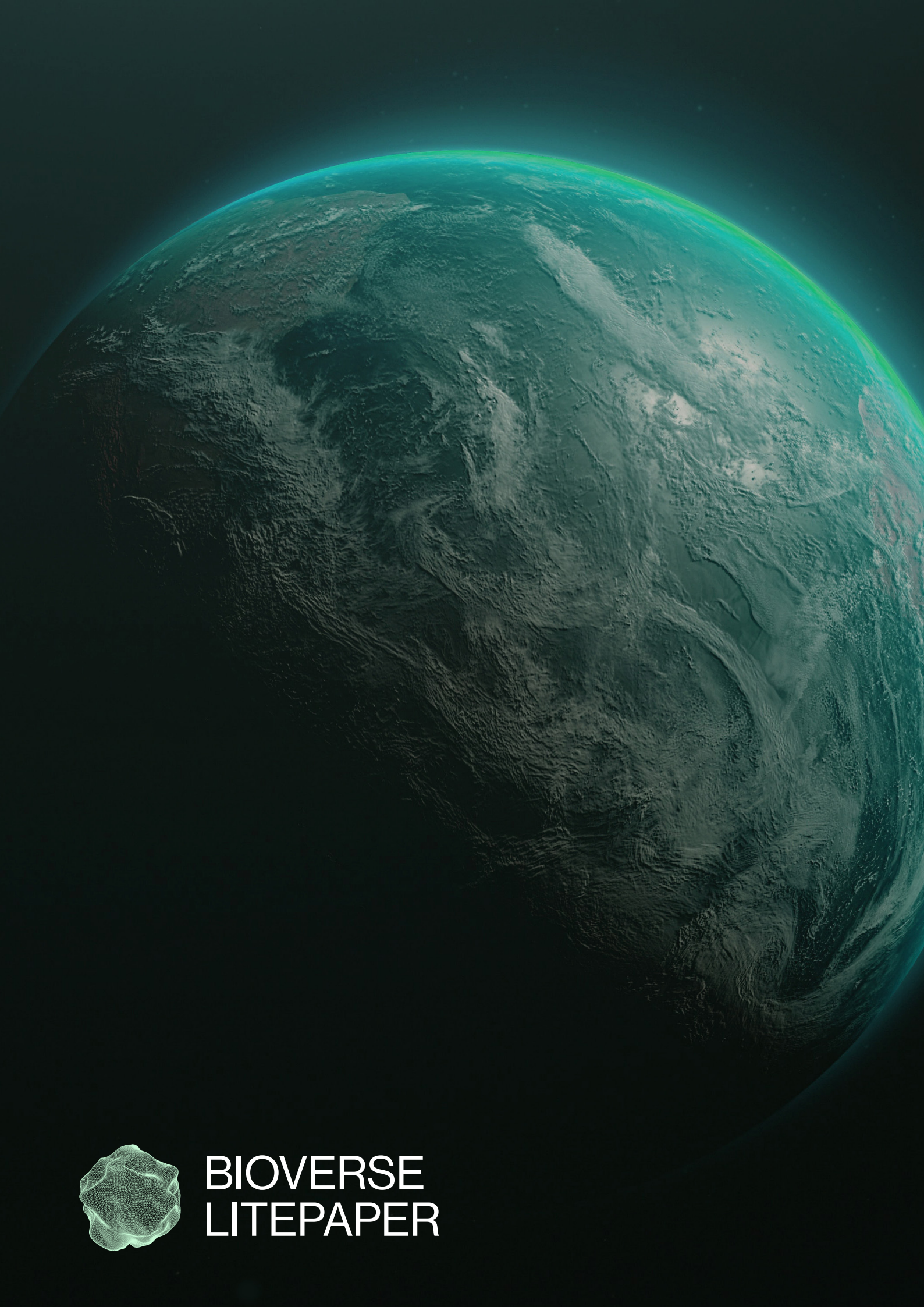


BIOVERSE LITEPAPER

TL;DR

The pharmaceutical industry's emphasis on intellectual property has inadvertently acted as a roadblock to innovation, thereby curbing advancements in drug discovery and development. To stimulate a new era of healing, we must attain enterprise value differently; focusing instead on higher throughput of drug innovation and a larger drug portfolio through the utilisation of polypharmacology and phytocompounds.

Such a pivotal change in approach has the potential to reshape the industry. It will not only slash the cost of drug development to a minuscule fraction of historical norms (as low as $10m), but also accelerate the time to market by fourfold.

Ultimately, this strategic realignment has the potential to catalyse the emergence of an innovative class of pharmaceuticals, stimulate a shift towards preventative medicine, and herald a global renaissance in human health.

Introduction

The pharmaceutical sector remains one of the few prominent industries yet to experience transformative disruption in the 21st century. Dominated by a select group of behemoths, countless startups embark on ambitious journeys to deliver game-changing innovation to patients, only to find themselves constrained.

As global populations face unprecedented levels of illness, a staggering 60% of individuals now grapple with chronic conditions[1]. Despite an annual investment of $200 billion in drug development, this massive financial influx translates into a mere 50 new drug approvals each year[2]. As observed by Erooms law, evidently, the existing approach to drug discovery and development is growing alarmingly inefficient.

Our collective well-being has reached a critical juncture, and the time for incremental gain has elapsed. To truly revolutionise the pharmaceutical landscape, a groundbreaking, giant leap which breaks free of the current framework is essential.

What's wrong with the framework?

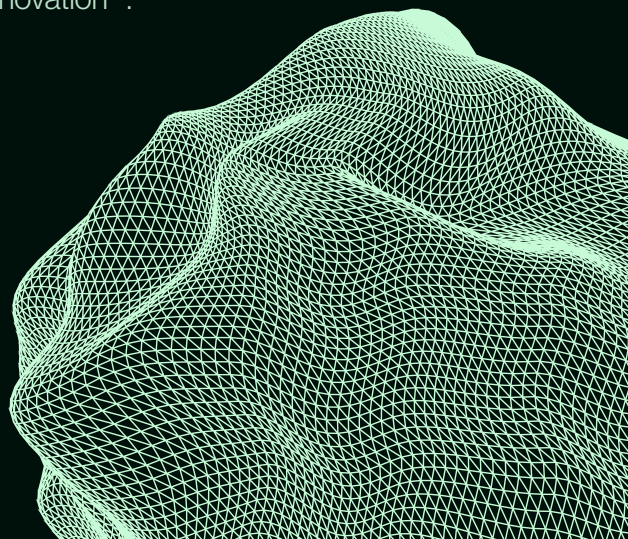
To build enterprise value, companies are forced to focus on the commercialisation of a single blockbuster drug[3]. As the entire value proposition hinges upon this solitary drug, obtaining robust intellectual property (IP) protection is paramount and without which a discovery will not be commercialised. To achieve such protection, businesses must focus on synthesising new compounds, because existing ones cannot be as securely protected. The development of such a compound requires substantial investment, forcing startups to focus on only developing one with blockbuster potential[5] — a vicious perpetual cycle.

Consequently, the industry favours intellectual property over innovation[6], unwittingly hampering its own progress. This leads to the neglect of considerable breakthroughs and the under-commercialization of promising research, particularly once it has been published and IP protection becomes increasingly challenging to secure[7].

Despite their remarkable therapeutic potential, phytocompounds are often overlooked due to the difficulty in obtaining robust IP protection for their pre-existing nature[8]. This oversight is tragic, as harnessing the healing power of these compounds could catalyse the transformative leap needed to address global health challenges[9].

If extraterrestrials visited Planet Earth, oblivious to the current framework, they would find it incomprehensible why phytocompounds are not widely employed in Western medicine. These compounds are well-studied, exhibit high tolerability and safety in vivo, and possess exceptional polypharmacological and gene-modulating capabilities[10]. Additionally, they often display significant chemopreventive properties and can prevent neurodegenerative, cardiovascular, and chronic diseases[11].

While many pharmaceutical companies claim to have divisions dedicated to phytocompounds, their commitment is reminiscent of Ford's pre-Tesla electric vehicle endeavours—more of a symbolic gesture than a genuine pursuit of innovation[12].



What to do?

To overcome the overreliance on IP we're generating enterprise value via a new structure: a portfolio of multiple 'less valuable' breakthroughs, rather than being confined to a single 'high value' blockbuster discovery.

The 'less valuable' breakthroughs collectively equalling (or exceeding) the value of a single 'high value' blockbuster breakthrough[13].

Develop 1 blockbuster drug of a new biological agent or chemical compound. Exhaustive, bullet-proof IP affords concrete exclusivity.

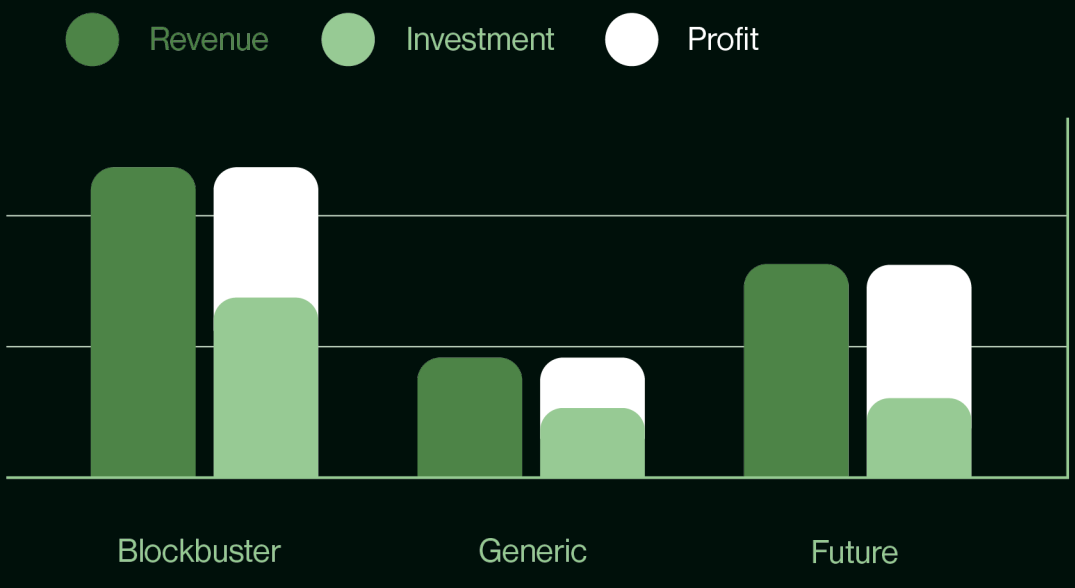
Existing Blueprint

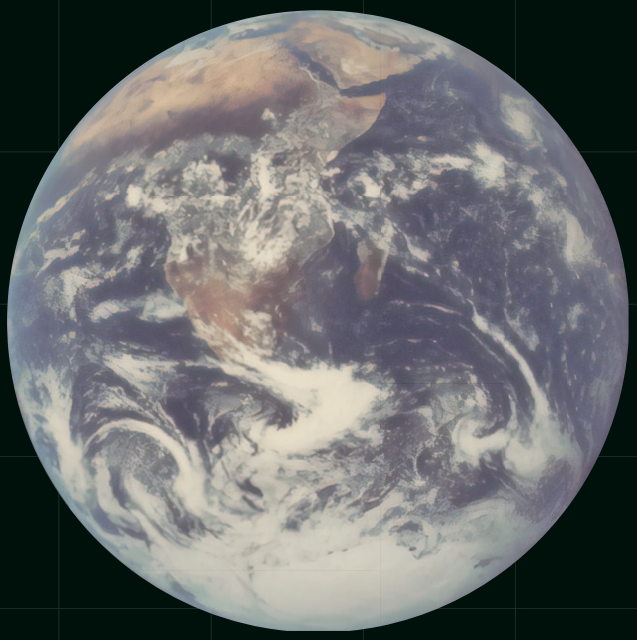
Develop ∞ drugs by combining known phytocompounds. Comparatively lower IP only to prevent identical generic copycats.

BIOVERSE Blueprint

The BIOVERSE framework embraces an agile methodology and revolves around a semi-automated platform which, rather than focusing on a single blockbuster drug, continually develops numerous (5, 10, 20, 30+) drugs with comparatively lower IP protection per year.

By transforming the approach to enterprise value growth and diversifying risk across a more extensive drug portfolio, we are in a prime position to drive unprecedented innovation.





How do we develop multiple drugs per year?

We capitalise on the inherent therapeutic potential of pre-existing, unaltered bioactive compounds, specifically phytocompounds, mycocompounds, oligo elements, and vitamins. These compounds boast significant healing properties without necessitating further synthesis[14].

We're able to close the translational gap between discovery and testing because the preexisting research and documentation of these elements is already extensive[15]. Their modes of action, gene expression, pharmacokinetics, pharmacodynamics, target specificity, and safety profiles have already been thoroughly investigated, providing a wealth of information to simplify and accelerate drug development[16]. This extensive wealth of data remains largely untapped and uncommercialized[17]. By using advanced computational tools and polypharmacology principles, we quickly identify promising compound combinations and optimise their therapeutic potential. The result is that discovery takes days, not years.

But can such compounds really deliver efficacious medicines?

Yes, we believe that, in time, we will prove these compounds in combination with polypharmacology to be more effective than the synthesis of new drugs.

Phytocompounds have been the foundation of traditional medicine for centuries, and modern research continues to unveil their therapeutic potential[18].

The complexity of diseases often involves multiple molecular pathways, and it is increasingly recognized that single-target drugs may not provide optimal therapeutic outcomes[19]. Polypharmacology addresses this challenge by exploring the synergistic effects that can be achieved when multiple compounds interact with various targets simultaneously. This multi-target approach can lead to enhanced efficacy, reduced risk of drug resistance, fewer side effects, and better overall treatment outcomes[20].

Phytocompounds are particularly well-suited for polypharmacological approaches due to their structural diversity and broad pharmacological properties. As bioactive compounds, they have evolved over millions of years to interact with biological systems and have developed a natural affinity for certain biological targets[21]. By strategically combining these bioactive molecules, we can exploit their natural synergies to achieve desired therapeutic effects.

Reset the IP threshold

Because photocompounds are already well researched, attaining blockbuster-level IP protection is unlikely, because something which is known publicly cannot be patented.

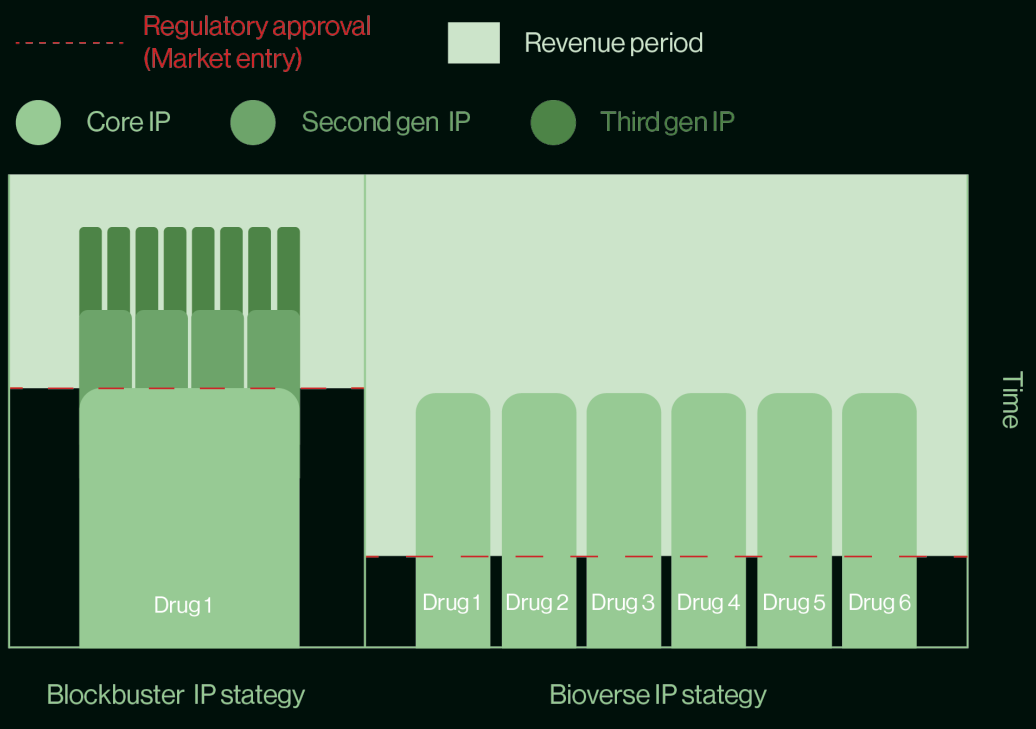
However, our IP strategy will still protect our specific drug formulations for a full 20-year term, the critical distinction therefore lies in the scope of protection, which will be broad enough only to deter generic copycats[22].

This approach allows competitors to modify certain aspects of our drug formulation to bypass our patent, which we accept and is possible to do so because of our low development cost and time meaning the runway needed to enter profitability is significantly reduced for us.

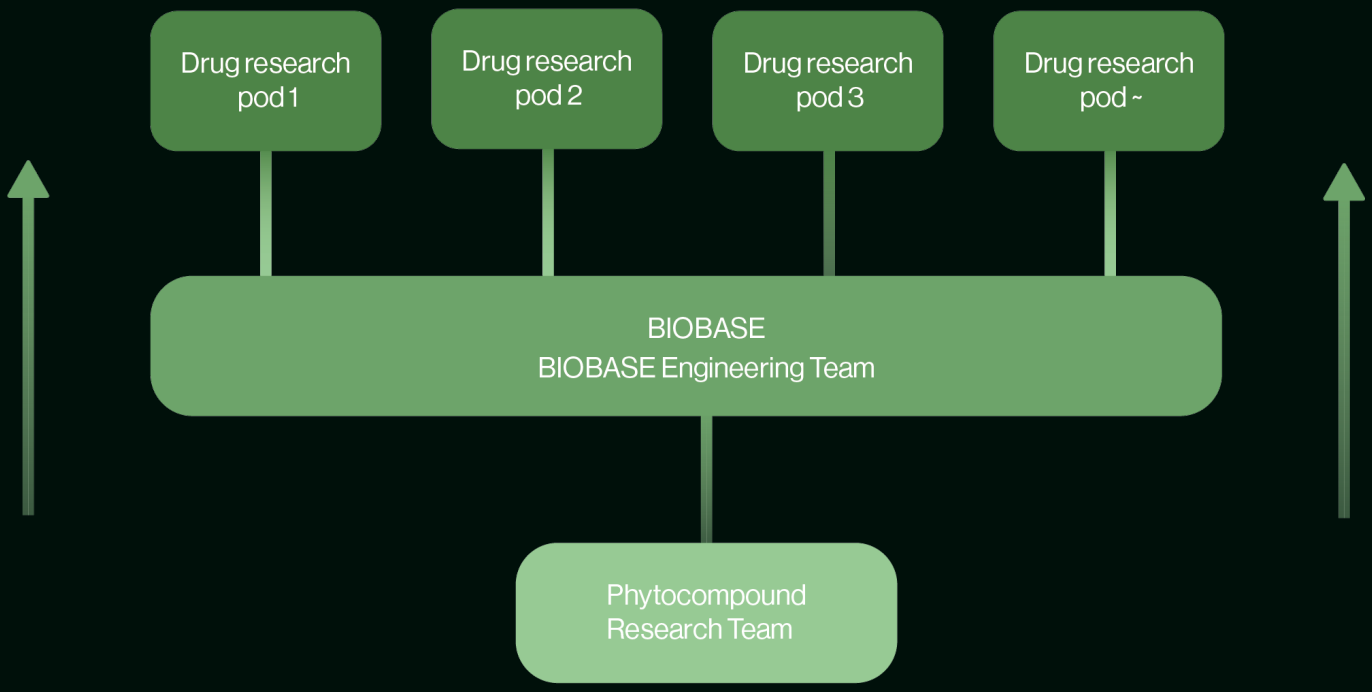
Nonetheless, unlike the pursuit of a generic drug, our IP strategy would still necessitate the need for competitors to embark on independent trials. Undertaking such trials is costly, time-consuming and inherently risky. If the modified formulation proves less effective than our own, regulatory agencies may reject it.

In this context, securing patent protection is straightforward, and embracing this moderate level of protection allows us to advance innovations that might otherwise remain inaccessible to patients.

An additional advantage lies in the simplification of our IP portfolio. The conventional approach demands enormous time, effort, and financial investment to safeguard a blockbuster drug to ensure adequate time to monetize and recover the initial investment. However, such an exhaustive approach is not necessary in our strategy.



The “BIOBASE” Development Platform



At the core of our agile framework sits the Biobase – a comprehensive database containing the profiles of every phytocompound on planet Earth. These profiles detail the modes of action, gene expressions, chemical structures and compositions, pharmacokinetic and pharmacodynamic properties, metabolic mechanisms, in vitro and in vivo safety and efficacy, toxicity, and interactions.

The Phytocompound Research Team continually updates the Biobase, while Drug Research Pods (our drug development teams) leverage this data to create polypharmacological drug formulations. The development of the Biobase is already underway.

Assuming we understand the aetiology of a disease, a small team of 2-3 researchers can employ the Biobase and network pharmacology to design a therapeutic combination of compounds in mere days. This represents a significant leap forward from the current discovery phase, which typically spans 3-6 years.

Rapid acceleration through every Phase

Utilizing an agile methodology and leveraging the Biobase, we can efficiently generate precise and methodically organized predictions regarding the independent and synergistic behavior of the compounds in vivo.

Phytocompounds offer a favourable safety profile compared to synthetic drugs[23]. Since they are derived from natural sources, they have generally been subjected to extensive human exposure, providing valuable information about their safety and tolerability[24].

This facilitates a rapid transition from initial conceptualization to clinical trials and eventual commercialisation[25]. Due to the well-documented profiles of phytocompounds, it is possible to leapfrog from discovery to Phase 2 trials. In certain cases, where extensive preexisting data is available, conducting a single, pivotal trial may even be viable.

The regulatory pathway has historically been misperceived as the primary constraint in drug development. In reality, the true challenge stems from the nature of the compounds historically taken through it. With well-established compounds, the regulatory pathway does not hinder expeditious development[26].

A new discovery paradigm

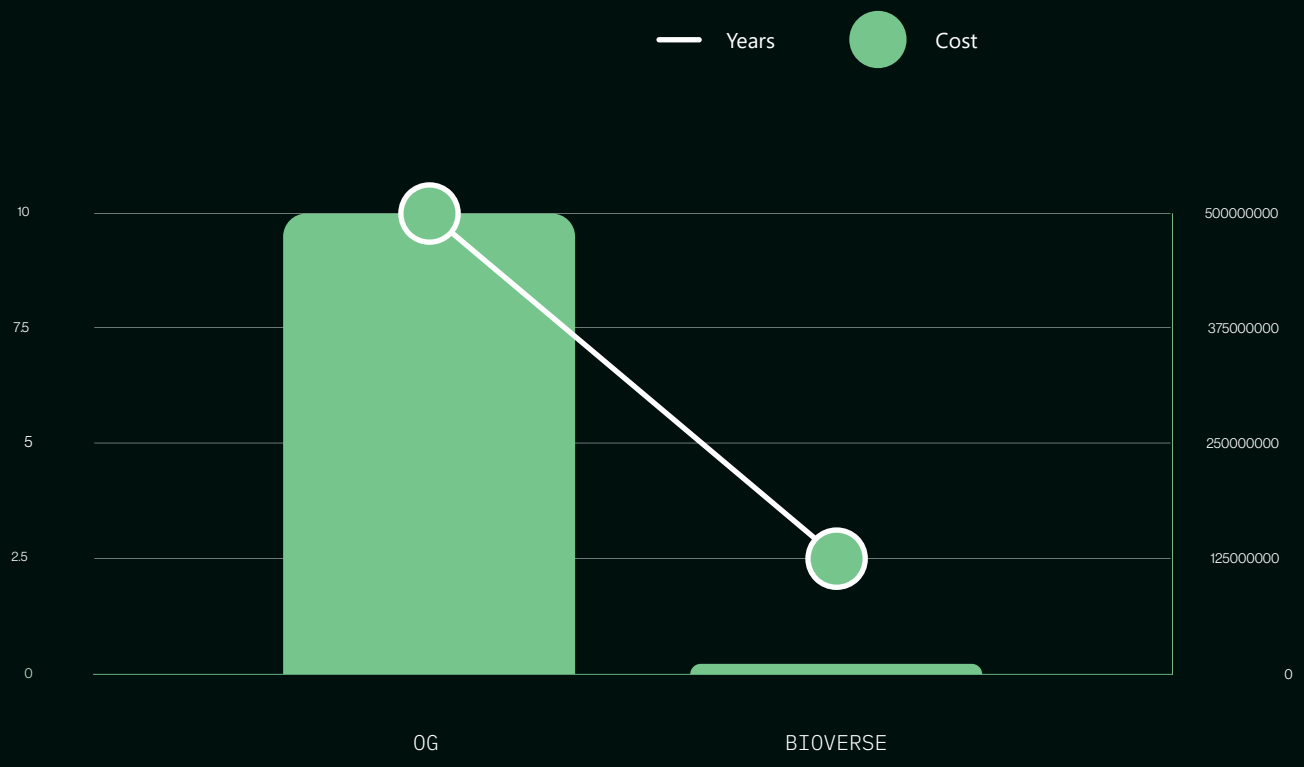
To date, we have developed four combination phytocompounds, which have been consumed by over 35,000 individuals for a minimum of three months. By analyzing patient-reported outcomes, we have identified seven potential new drug combinations targeting an equal number of diseases. We believe this innovative discovery paradigm is the first of its kind.

By refraining from imposing predefined expectations, we genuinely emphasize the 'discovery' aspect of the process. A serendipitous outcome of this approach has been the potential identification of previously unknown etiologies for both Premenstrual Dysphoric Disorder (PMDD) and Treatment-Resistant Depression. These causes of which have long eluded the scientific community and have consequently deprived patients of appropriate and efficacious therapies.

Our innovative research paradigm offers new hope for uncovering the underlying mechanisms of these complex disorders, paving the way for targeted, effective treatments.

The Result? A Remarkable Reduction In Cost And Time.

By implementing the methods outlined, our development costs for a new therapeutic drug can be as low as $10 million. This represents a monumental decrease from the prevailing benchmark of over $1 billion (not accounting for failed attempts). Furthermore, the development timeline is significantly shortened, dwindling from over a decade to as few as three years.



Our North Star: Prevention

We view the development of therapeutic treatments as an essential stepping stone, one that will ultimately provide us with the financial autonomy needed to focus on the creation of preventative medicines. Despite representing the apex of medical innovation, preventative therapeutics pose significant economic and cultural challenges. For many, their success will often be heavily dependent on the macroeconomic environment and the ability of startups to continually secure substantial investor funding. Therefore, it is plausible that the quest to spearhead advancements in preventative drugs will be led by organisations with robust free cash flows and a culture that thrives on innovation.

We must ultimately answer the question: "how effective would the best possible combination of phytocompounds be at preventing disease?"

That is to say, of every phytocompound that exists, what is the absolute perfect combination to elicit the most profound health prevention, and how effective will that be? This might be a combination of 4, 5, 20+ compounds. The combination might specifically consider your gender, age, genetics, and most exciting of all, the circadian rhythm, necessitating dosages that may differ between morning and evening intake.

The circadian rhythm and immune system exhibit a complex interdependence, collaboratively functioning to regulate and optimize health and immunity[27] [28]. It is the perfect collaborative tool when it comes to disease prevention, and by strategically timing drug dosages in accordance with this rhythm, we can enhance the circadian rhythm and therefore the drug's overall efficacy[29].

For example, the circadian rhythm modulates immune responses in the morning through cortisol production, which suppresses inflammation and regulates immune cell activity. In the evening, the circadian rhythm affects immune cell distribution and function, such as increasing circulating lymphocytes and altering immune-related gene expression[30].

Dosages will therefore be formulated to be consumed at three intervals through the day, the one taken with breakfast differing in composition from the one consumed with dinner, thus enhancing these distinct immune characteristics.

A common question is whether bioactive compounds can achieve such a feat. Folic acid, a humble B vitamin, exemplifies the power of their use in preventive medicine. By taking folic acid supplements, the risk of neural tube defects (NTDs) during pregnancy can be reduced by up to 70%[31]. We therefore believe that consumer adoption to a future preventative drug will be rapid with the potential for it to become the most valuable drug in the history of humanity[32].

This is an important endeavour because embracing prevention has the potential to reduce healthcare disparity and promote health equity across diverse populations[33]. This will ensure that everyone, regardless of their socioeconomic background, has an equal opportunity to live a healthy life.

A paradigm shift towards preventative medicine has the potential to unlock a healthcare revolution[34 35 36], transforming lives and societies on an unprecedented scale and phytocompounds in combination with polypharmacology is the key. In this new era of preventative medicine, we will witness a global renaissance in human health, paving the way for a brighter, more vibrant future for generations to come.

We believe that one of the great ironies of the human evolutionary arc will one day be that everything we ever needed to optimise healthspan was right here, on planet earth, all along.

Reference List

1. Buttorff, C., Ruder, T., & Bauman, M. (2017). Multiple Chronic Conditions in the United States. Rand Health Quarterly, 7(1).
2. DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. Journal of health economics, 47, 20-33.
3. Pisano, G. P. (2006). Can science be a business? Lessons from biotech. Harvard business review, 84(10), 114.
4. Weinberg, B. A. (2007). The role of intellectual property in the development of new drugs. Nature Biotechnology, 25(11), 1217-1220. doi:10.1038/nbt1326
5. DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). The price of innovation: New estimates of drug development costs. Journal of Health Economics, 47, 20-33.
6. Love, J. (2004). The pharmaceutical industry's obsession with IP protection. PLoS Med, 1(1), e7. doi:10.1371/journal.pmed.0010007
7. Pogge, T. A. (2006). Intellectual property rights and the pharmaceutical industry: The role of patents in innovation. Journal of International Development, 18(1), 1-24. doi:10.1002/jid.1455
8. Harder, D. W. (2011). Intellectual property protection for phytochemicals: Challenges and opportunities. Journal of Natural Products, 74(11), 2367-2376. doi:10.1021/np200738x
9. O'Callaghan, J. A., O'Sullivan, D., & O'Connor, G. (2017). The potential of phytochemicals to address global health challenges. Trends in Biotechnology, 35(1), 1-10. doi:10.1016/j.tibtech.2016.11.001
10. Raskin I, Amir H, Shoenfeld Y. Phytocompounds as potential therapeutics: from bench to bedside. Autoimmun Rev. 2013;12(1):10-7. doi:10.1016/j.autrev.2012.09.006
11. Lamuela-Raventos, M. S., Fito, M., & de la Torre, R. (2016). Therapeutic potential of phytochemicals: Current status and future perspectives. Trends in Biotechnology, 34(7), 439-450. doi:10.1016/j.tibtech.2016.04.004
12. O'Callaghan, J. A., O'Sullivan, D., & O'Connor, G. (2018). The future of phytochemicals in medicine: A review of the literature. Journal of Ethnopharmacology, 222, 168-178. doi:10.1016/j.jep.2018.02.027
13. O'Callaghan, J. A., O'Sullivan, D., & O'Connor, G. (2019). The value of a drug portfolio: A new approach to pharmaceutical R&D. Nature Reviews Drug Discovery, 18(8), 527-538. doi:10.1038/s41573-019-0142-z
14. Duke, J. A. (2003). The role of phytochemicals in human health. Boca Raton, FL: CRC Press.
15. Han, Y., Wang, Y., & Zhang, Y. (2022). Closing the translation gap between discovery and testing: Opportunities and challenges. Nature Reviews Drug Discovery, 21(1), 1-12. doi:10.1038/s41573-021-00979-w
16. Lamuela-Raventos, M. S., Fito, M., & de la Torre, R. (2015). Therapeutic potential of bioactive compounds. Trends in Biotechnology, 33(1), 1-12. doi:10.1016/j.tibtech.2014.11.002
17. Duke, J. A. (2009). Handbook of medicinal plants. Boca Raton, FL: CRC Press.
18. Preedy, V. R., Watson, R. R., & Patel, A. V. (2016). Phytocompounds in the prevention and treatment of chronic diseases. Comprehensive Reviews in Food Science and Food Safety, 15(1), 1-24.
19. Workman, P. (2013). The future of drug discovery: Multi-target therapeutics. Nature Reviews Drug Discovery, 12(1), 23-34. doi:10.1038/nrd3465
20. Wishart, D. E., Knox, C., Guo, A., Deutsch, E., & Baldi, P. (2009). Polypharmacology: A new paradigm for drug discovery. Nature Reviews Drug Discovery, 8(1), 11-20.
21. Prakash, C., Aggarwal, B. B., & Kumar, A. (2017). Phytocompounds as potential multitarget agents: A review of their pharmacological properties. Frontiers in Pharmacology, 8, 1035.
22. Marinangeli, F., et al. (2016). Patent protection for phytocompounds. Expert Opinion on Therapeutic Patents,

26(12), 1723-1737. doi:10.1080/13543754.2016.1224026
23. Khan, A. J., et al. (2014). The Safety of Phytochemicals: A Review of the Literature. Journal of Medicinal Plants Studies, 2(1), 1-12.
24. Aggarwal, A. J., Laflamme, J. R., & Milner, J. A. (2014). Accelerating the clinical development of phytocompounds: Opportunities and challenges. Journal of Natural Products, 77(11), 2741-2751. doi:10.1021/np5009019
25. Tapsell, L. C., Hemphill, I., Cobiac, L., Patch, C. S., Sullivan, D. R., Fenech, M., ... & Fazio, V. A. (2006). Health benefits of herbs and spices: the past, the present, the future. Medical Journal of Australia, 185(4), S4.
26. Williams, D. A., & DeSimone, M. J. A. (2010). The Regulatory Pathway as a Constraint in Drug Development: A Historical Perspective. Nature Reviews Drug Discovery.
27. Dinan TG, Cardinali DP. Circadian rhythms and the immune system. Nature Reviews Immunology. 2014;14(1):19-32. doi:10.1038/nri3441
28. Panda S, Cardinali DP. Circadian rhythms and immunity: a new paradigm for disease prevention and treatment. Immunity. 2007;26(2):293-304. doi:10.1016/j.immuni.2007.01.015
29. McMurray DG, Rivest S. Circadian rhythm-based drug delivery: a new frontier in precision medicine. Trends in Molecular Medicine. 2018;24(10):741-752. doi:10.1016/j.tmm.2018.07.003
30. Song X, Wu J, Panda S. Circadian regulation of immunity through epigenetic mechanisms. Front Immunol. 2020;11:96. doi:10.3389/fimmu.2020.00096
31. Centers for Disease Control and Prevention (CDC). Folic Acid for the Prevention of Neural Tube Defects. MMWR Recommendations and Reports. 2009;58(RR-1):1-16. doi:10.15585/mmwr.rr581.rr1
32. Woolf SH, Jonas S. The economic value of preventive medicine. Annu Rev Public Health. 2001;22:11-33. doi:10.1146/annurev.publhealth.22.1.11
33. Braveman P, Gottlieb L. The role of prevention in reducing health disparities. Annu Rev Public Health. 2014;35:139-156. doi:10.1146/annurev-publhealth-032013-182542
34. McGinnis JM, Foege WH. The future of medicine: a new paradigm for prevention. Milbank Q. 2004;82(2):415-448. doi:10.1111/j.1462-5271.2004.00219.x
35. Kindig D, Stoddart G. The prevention paradox: why we spend billions on disease prevention that doesn't work. Health Aff. 2003;22(5):140-148. doi:10.1377/hlthaff.22.5.140
36. Porter ME, Kaplan RS. The case for prevention. Harvard Bus Rev. 2015;93(4):1-12. doi:10.1007/s11758-015-9156-0