EXECUTIVE SUMMARY

Strategies for Synbio Success

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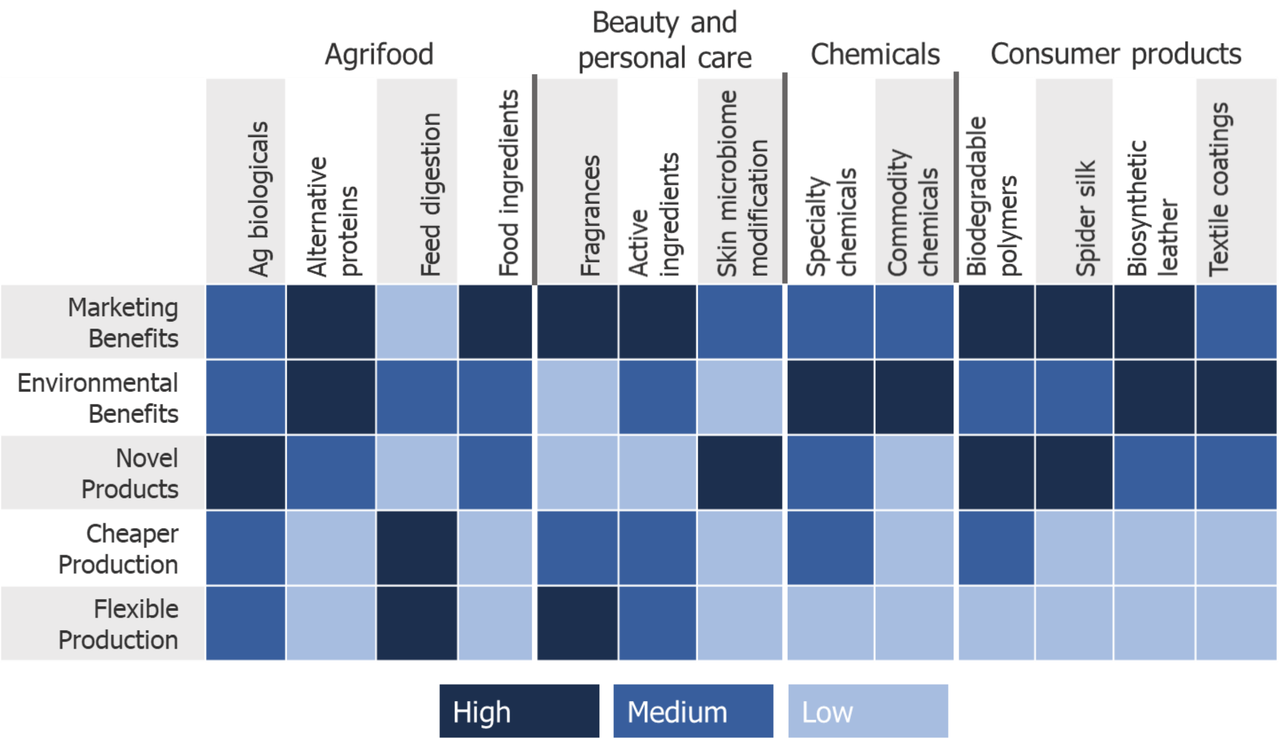
Executive Summary

Synthetic biology (synbio) has emerged as an alternative to traditional petrochemical synthesis for applications in agrifood, beauty and personal care, chemicals, and consumer products.

Effectively using synbio capabilities requires understanding the right strategy for each of the distinct value propositions it can offer, including marketing benefits, environmental benefits, novel products, cheaper production, and flexible production.

As the next decade unfolds, synbio strategy will evolve from creating niche products with "green" credentials, to creating new molecules not accessible with current tech, to developing new capital-light business models based on strain development and fermentation as a service.



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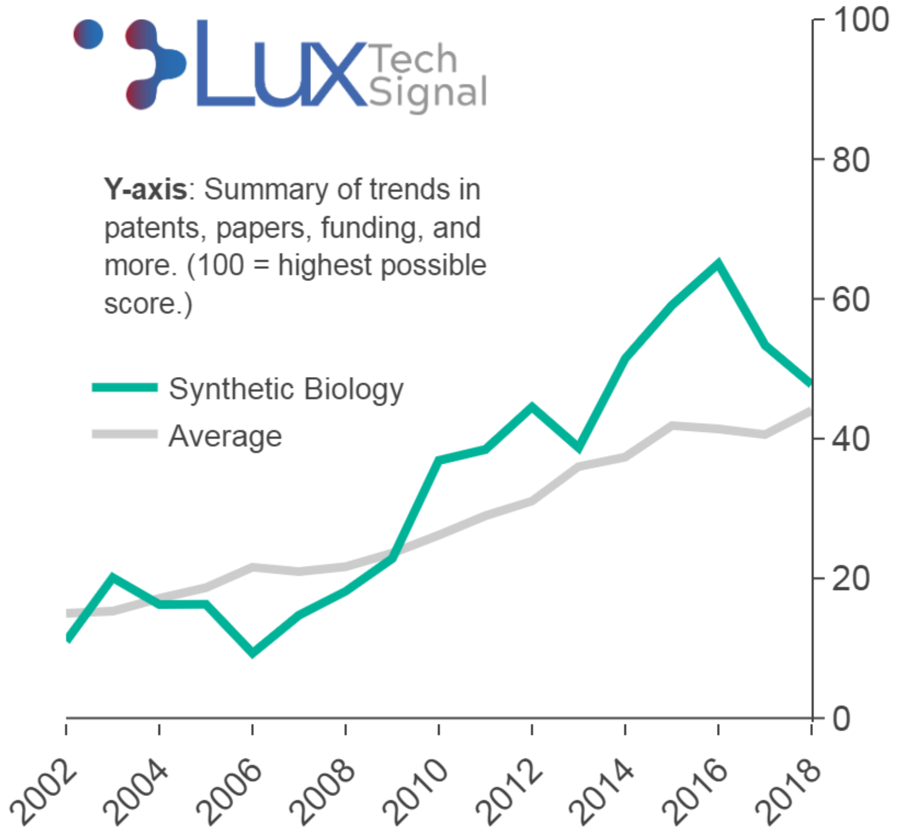
Synthetic biology has high potential as an alternate production route for chemicals

While traditional petrochemical synthesis has led to the commercial-scale production of numerous chemicals and materials, the limitations of the technology, as well as the its (real and perceived) ill effects, have led researchers to explore biological routes instead. Biological catalysts (enzymes) offer better reaction rates, selectivity, and yields; don't require high temperatures or pressures; and can convert biomass, waste, or other more environmentally friendly feedstocks – all while offering a patina of "natural" biological origin.

Over the past decade, biological tools from genetic engineering to DNA synthesis have been developed to enable the creation of organisms that use fermentation to produce a variety of desired molecules from sugars or other biological feedstock. As a result, interest and activity in this approach, called *synthetic biology* (or synbio), has grown, creating billion-dollar companies and generating a flurry of innovations.



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Despite its promise, synbio isn't for everything

Not all syntheses are amenable to fermentation; a targeted use might not be a fit for one of two reasons:

Microorganisms may not be able to metabolize the desired feedstock. While this may provide a challenge for some feedstocks, such as crude oil, microbes naturally metabolize sugar to produce a wide variety of chemical targets – and many types of biomass can be converted to sugars.

Genes may not exist to produce the target compound. Although microbes can be readily genetically modified to produce a wide variety of compounds, some lack the genetic code for production. It may be possible to develop the necessary genes, but some molecules are more accessible than others.

Synbio works particularly well for:

- *Naturally occurring products*. If genes for the target are found in nature, it requires less effort to make via microbial fermentation.
- *Enantiopure products*. Biological catalysts are highly effective at producing just one of two possible mirror images of a molecule, often important for drugs and other active ingredients.

Synbio does not work as well for:

- *Inorganic compounds.* Microbes are generally best at converting a carbon source to a carbon-containing product.
- *Hydrocarbons.* Most fermentation feedstocks are oxygenated carbon compounds – from sugar to CO_2. Making pure hydrocarbons is less efficient due to the need to remove oxygen.

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Synbio offers a range of value propositions in industrial and consumer applications

The ability to engineer microbes to produce chemicals on command is heady stuff for a technologist, but what is the business case for using a synbio approach over long-established traditional synthetic chemistry? From our conversations with key players, ranging from startups to large companies across a variety of industries and regions, we've identified the following value propositions:

- **Marketing benefits**: Products can be marketed as "natural" or "bio-based," without emphasizing environmental advantages
- **Environmental benefits**: Routes have decreased environmental impacts over incumbent routes, especially with respect to decreased carbon footprints
- **Novel products**: For certain applications, synbio can make products that have no existing manufacturing route; these products may have improved performance over incumbent products, but do not necessarily
- **Cheaper production**: Synbio routes can result in cheaper costs relative to incumbents
- **Flexible production**: Simply switching out the microbes in a given fermenter means producing a new compound with equipment changes or plant redesign, allowing for small-volume production of numerous different compounds and/or changing production based on market demand

The full report dives into each of these key value propositions.

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ROUTES HAVE DECREASED ENVIRONMENTAL IMPACTS OVER INCUMBENT ROUTES

Value Proposition: Environmental Benefits

JOYN BIO

How does synbio enable this?

Fermentation processes use renewable feedstocks as opposed to petroleum, and production can have decreased environmental impacts, including a reduced CO_2 footprint and less use of toxic compounds.

Challenges

Companies have struggled to commercialize environmentally friendly products in the past, leading to challenges with internal interest. Some processes may use more energy and water than incumbent routes.

Target applications

Reduced environmental impact has been used as a value proposition across most target industries for fermentation, notably chemicals, textiles and apparel, and agrifood.

Key Developers

IMPOSSIBLE™	Synbio-derived leghemoglobin uses 96% less land and 87% less water and results in 89% fewer GHG emissions compared to beef
Braskem	Claims fermentation-derived PE removes CO_2 from the atmosphere

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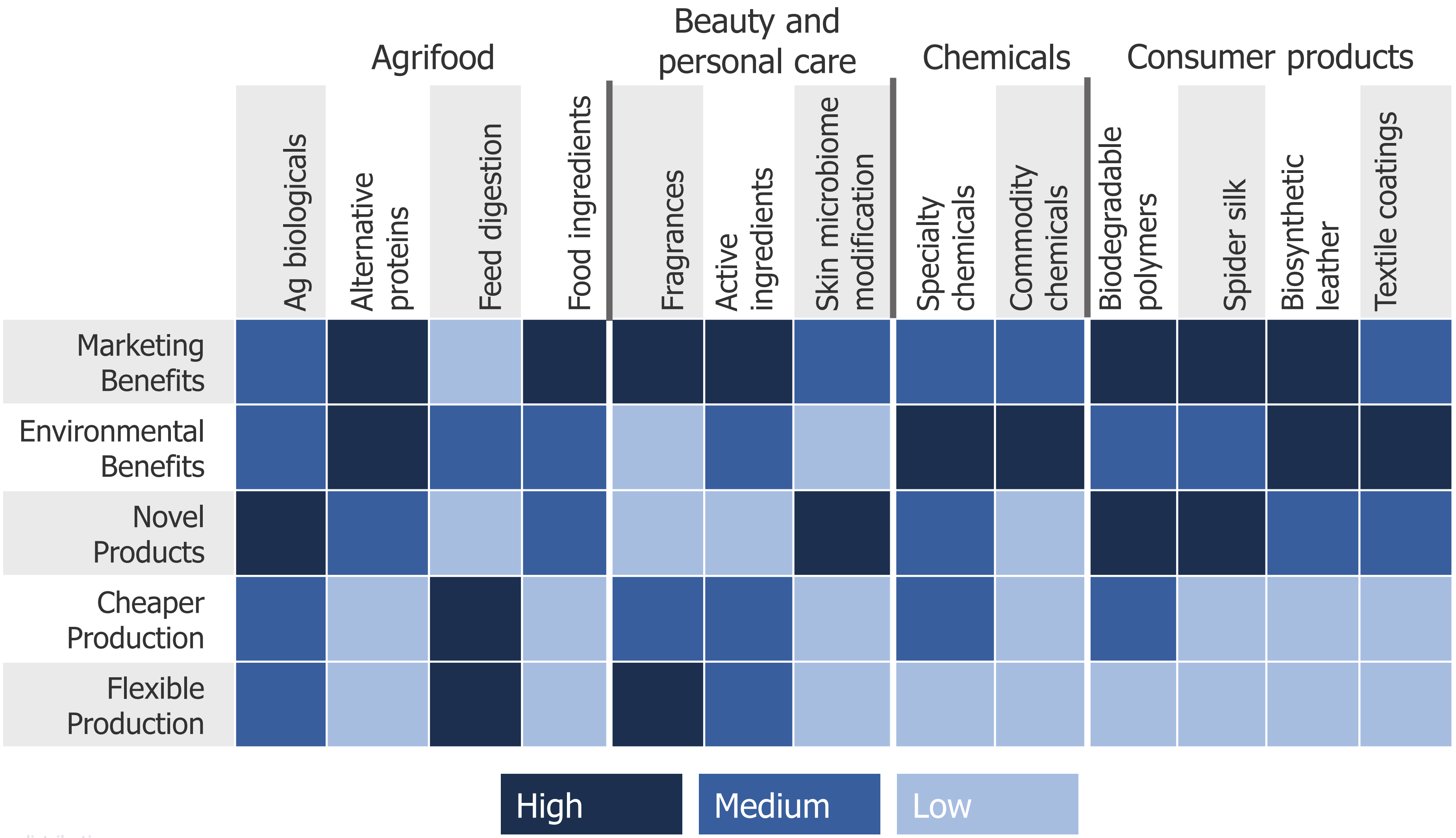
Marketing and environmental benefits dominate the value proposition applicability across all industries



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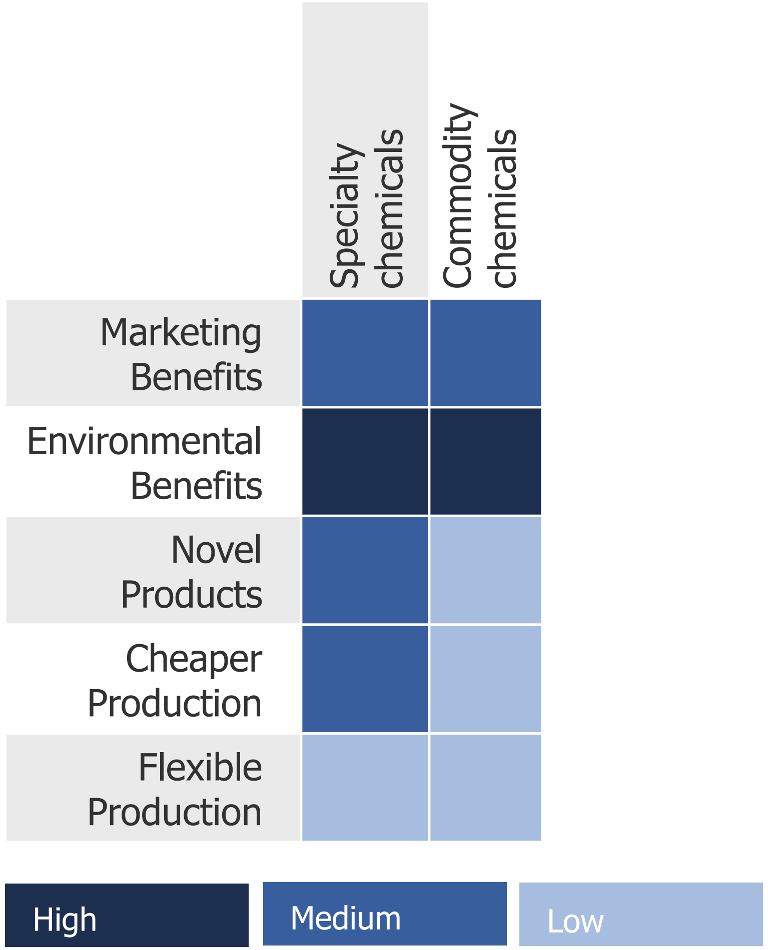
Environmental benefits are the best value proposition for chemicals, with cost relevant in some cases



In chemicals, environmental benefits stand out as the most applicable value proposition for fermentation routes. The prospect of using biomass as an input for chemical production can reduce CO_2 emissions and help drive adoption in an industry undergoing increasing scrutiny for poor environmental footprints.

Given that specialty products are smaller-volume, there is potential for cost reduction of existing products, exemplified by Genomatica, which uses cost reduction as a value proposition for its 1,4-butanediol and caprolactam.

There are some opportunities to develop novel chemicals using fermentation, such as succinic acid and furandicarboxylic acid (FDCA). Novel chemicals are best targeted for specialty applications, as challenges with scale and market development have led to numerous failures for those targeting commodity chemicals from fermentation.

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KEY STRATEGIES

Value Proposition: Flexible Production

There are two key strategies for flexible production. The first is imitating contract manufacturing organizations (CMOs) – or semiconductor fabs – in providing production services to other companies. Companies can specialize either in developing their own strains or in running those strains on fermenters in flexible facilities, maximizing capital efficiency and leveraging each type of expertise separately.

The second is using synbio's flexibility to optimize and arbitrage one's own product portfolio, either using a single fermenter to make a year's worth of different products over a short amount of time or changing microbes at a given fermenter depending on market demands. The latter strategy would require either having a library of strains on hand or the ability to rapidly develop strains.

Additionally, companies could use feedstock flexibility to expand to regions with different input availability.

CASE STUDY: Conagen

Introduction

Strain developer Conagen recently announced it developed strains to produce upward of 20 rare lactones for flavors and fragrances.

Use case and business impact

While Conagen has not yet produced any of these lactones at commercial scales, similar downstream processing conditions allow flexible production at scale.

LUX TAKE

Conagen is well-positioned to use the flexible production value proposition for its lactones – these products are small-volume and used in the same applications. However, the biggest unknown is whether or not Conagen will need to use flexibility. If market demand is skewed toward a small fraction of the lactones, flexibility becomes less relevant.

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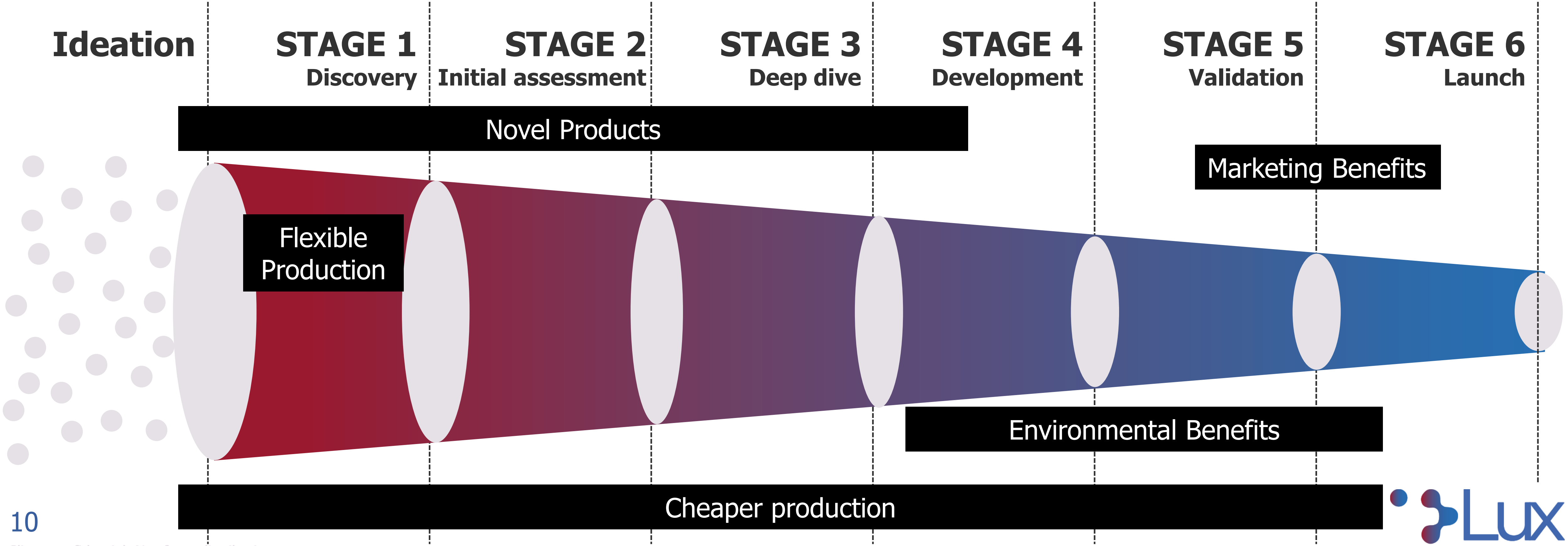
Different value propositions for synbio have different stages of maturity

Setting out a full synbio strategy requires understanding not just *how* to act but *when* – and different value propositions will be realized at different times, as this mapping to the innovation funnel shows. The following slides show how these benefits will combine to shape three stages of synbio's growth.



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2020-2025: First developed products come to market

What will happen: Over the first half of the 2020s, small-volume products using marketing benefits as a label will continue to launch. Because production is not well-established, the two most important factors in this validation phase are feedstock and infrastructure. Players that can establish a feedstock source and production capacity will beat out those that are unable to secure either. Due to the relatively low numbers of players, the microbe and market will not matter as much – the players that bring products to market are not competing with other fermenters, but with established markets.

Applications entering the market: Small-volume applications with minimal regulatory hurdles, such as beauty and personal care, will be first to market; others, such as food ingredients, will have opportunities to prosper if users can steer clear of regulatory issues. While markets must be developed for ag biologicals and biodegradable polymers, both applications have downstream interest.

Key value propositions: Marketing benefits will be the dominant value proposition, while environmental benefits will start becoming more important. Cheaper production will play a role in a few select cases where it’s most easily achieved.

Strategies for the future: At this stage of technical development, owning and operating a facility, rather than using contract manufacturing, will make the most sense. While outsourcing production is an appealing strategy that requires less upfront capital, the greater control and process knowledge from running one’s own facility is more likely to be successful when the technology is less mature.

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