India

Underweight *(no change)*

Highlighted Companies

Ami Organics Ltd

REDUCE, TP Rs714, Rs1282 close

Ami Organics holds a couple of psychedelic intermediates and medications in its portfolio. The company has achieved a 50-90% market share in molecules like trazodone. Trazodone is used to treat major depressive disorders, anxiety disorders, and difficulties with sleep. The introduction of SynBio psilocybin will affect Ami Organics' market share adversely.

UPL Limited

REDUCE, TP Rs754, Rs607 close

UPL has multiple nitrogen-based fertilizers in its portfolio like GoActiv seaweed filtrate, Ag Harvest, Cevo, Folium Juvenile, and Cremalga. SynBio nitrogen bacterium fertilizers from JoynBio and Pivot, which are more effective, efficient, and give higher crop yield, are likely to affect UPL's sales adversely.

Rallis India Ltd

REDUCE, TP Rs218, Rs225 close

Rallis India produces synthetic pyrethroid insecticides, including cypermethrins. Pheromone-based insecticides by Provivi are a green, non-toxic, and species-specific alternative to pyrethroids (under heavy scrutiny globally). These products are a threat to Rallis India.

Summary Valuation Metrics

P/E (x)	Mar22-A	Mar23-A	Mar24-F
Ami Organics Ltd	64.16	55.42	52.53
UPL Limited	14.06	12.81	10.91
Rallis India Ltd	26.65	47.59	32.01

P/BV (x)	Mar22-A	Mar23-A	Mar24-F
Ami Organics Ltd	8.91	7.77	7.08
UPL Limited	1.92	1.68	1.46
Rallis India Ltd	2.58	2.53	2.39

Dividend Yield	Mar22-A	Mar23-A	Mar24-F
Ami Organics Ltd	0%	0%	0%
UPL Limited	1.87%	2.05%	2.41%
Rallis India Ltd	1.33%	0.59%	0.87%

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Chemicals - Overall

Synthetic biology - the new frontier

- Synthetic biology is a combination of engineering and genetic engineering. Scientists make artificial DNA & get it printed at a cost of ~US$0.40/base pair.
- The global synthetic biology market is likely to grow at a 21.4% CAGR to touch US$75bn over CY23F-31F.
- It has wide applications, from chemicals to pharmaceuticals, and poses risks to the business model of diagnostics, pharma & agrochemical companies.

Synthetic biology is the future of agrochemicals & pharmaceuticals

Synthetic biology is the refinement of genetic engineering. Scientists write DNA to make blocks that are inspired by nature. The DNA can be printed by printing machines using basic products like glucose, guanine, adenine, thymine, and cytosine. Multiple companies make synthetic DNA, as per customer needs, with the cost as low as US$0.40/ base pair.

Synthetic DNA injected in live cells produce the desired proteins

Scientists get the DNA (which can generate the desired proteins), get it printed, and inject it in the pre-selected bacterium/yeasts. The inserted/new DNA has a selection marker like an antibiotic resistance gene in it. The bacteria/yeast with only original DNA of the bacterium/yeast is killed by the antibiotics. Only the bacteria/yeast with the artificial DNA survive because they have the antibiotic resistance gene in them (see Fig. 1) This artificial DNA produces proteins to be used in chemicals/ agrochemicals/ pharmaceuticals.

Synthetic biology usage – from diagnostics to chemicals to pharma

Insulin is the first example of the use of synthetic biology in pharmaceuticals. Artificial T-cells have been designed (these cells are a part of the immune system) to fight cancer. These are called CAR-T cells. Anti-depression and post-traumatic disorder drugs like Psilocybin can also be produced from the engineered strains of *S. cerevisiae* and *E. coli*. Multiple vaccines are being developed using this technology. Synthetic biology is also used in diagnostics, particularly in paper-based testing and phage-based diagnostics. Some of the chemicals that can be produced on a mass scale using synthetic biology are vanillin, 1,4-butanediol, bio-nylon and insecticides that can replace toxic pyrethroids, etc.

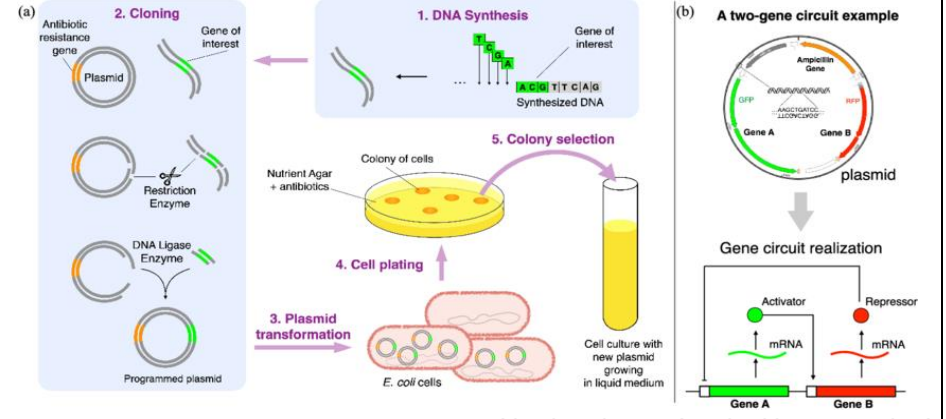
Various Indian companies are active in this field

Premas, Barcode Biosciences, and Saha Gene offer gene synthesis services in India. HiMedia Laboratories is an Indian pharmaceutical company that offers a wide range of raw materials for DNA synthesis. **ImmunoACT and Immuneel Therapeutics** are the two companies trying to commercialize the CAR-T cell product in India. Laurus Labs has a 33.86% stake in ImmunoACT. **Achira Labs** is developing a platform called Lab on Paper-based testing. Cipla acquired a 21.05% stake in Achira Labs in Jun 2022 for Rs250m.

Impact on the listed space

Multiple Indian chemical and pharma companies are at risk of obsolescence if they don't change their business ways. On the other hand, may be synthetic DNA coding and printing can become the future business outsourcing opportunity. However, we still don't have any listed name that is active in this space.

Figure 1: DNA is synthesized, cut, copied and pasted to genetically engineered cells



SOURCE: INCRED RESEARCH, COMPANY REPORTS

Synthetic biology

What is synthetic biology?

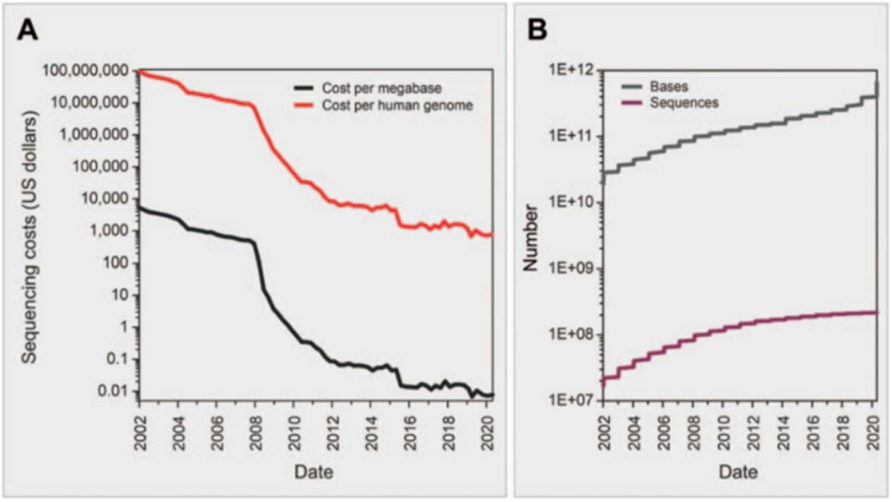
Synthetic biology is the refinement of genetic engineering. One can think of synthetic biology as a combination of engineering and genetic engineering. Scientists write the desired DNA in the form of code. DNA is made up of four chemical building blocks called nucleotides. These building blocks are made of three parts: a phosphate group, a sugar group, and one of the four types of nitrogen bases. The four types of nitrogen bases in DNA are adenine (A), thymine (T), guanine (G), and cytosine (C). These combinations are sent to DNA printers to print the desired DNA with the cost as low as US$0.40/base pair.

The DNA printing revolution

The basis of synthetic biology is synthetic DNA. With the advent of technology, instead of cutting DNA from one organism and pasting it into another, one can simply write the desired DNA sequence on a computer and order it from a website. Even though the DNA sequence is inspired by nature, the physical DNA itself is made by a machine and hence, synthetic DNA. The raw material for synthesizing DNA is readily available, such as sugar and the four DNA bases, fed in a modified version of an inkjet printer that prints the DNA. The cost of printing one base pair is **US$0.40,** and the price is reducing over time. The DNA product is freeze-dried and shipped to the customer's doorstep.

Several companies, like IDT, Genscript, Twist Bioscience, etc., provide this service. SGI DNA sells an instrument called BioXP that lets you print your synthetic DNA in your lab. **Premas**, **Barcode Biosciences**, and **SahaGene** offer gene synthesis services in India. **HiMedia Laboratories** is an Indian pharmaceutical company that offers a wide range of raw materials for DNA synthesis, including nucleotides, primers, and buffers. The company manufactures a variety of nucleotides, including deoxyribonucleosides (dNTPs), ribonucleosides (rNTPs), and nucleoside triphosphates (NTPs).

Figure 2: The cost of sequencing per base pair has gone down and the amount of DNA being sequenced has gone up with time



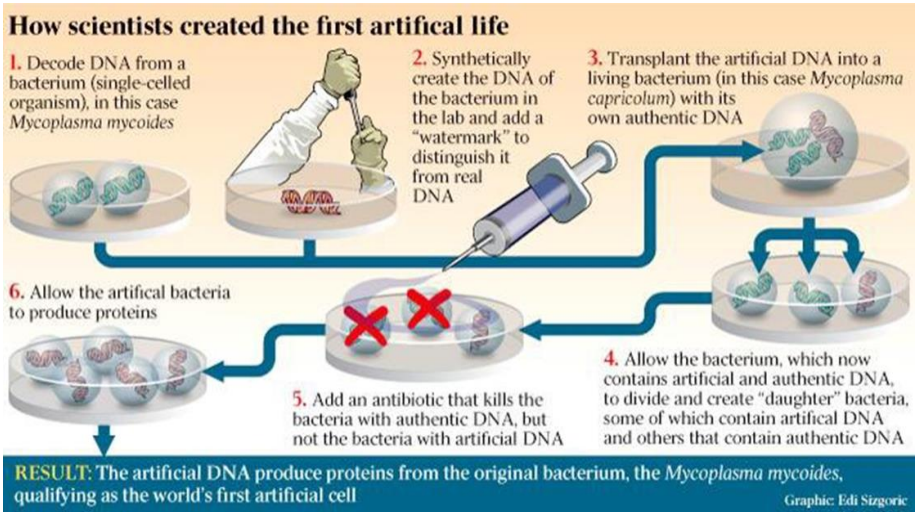
SOURCE: INCRED RESEARCH, COMPANY REPORTS

Synthetic biology can become an US$75bn market by CY31F

The global synthetic biology market is likely to grow at a 21.4% CAGR over 2023F-31F. It is expected to achieve a market valuation of US$ 74.7bn by the end of the forecast period. Even the big players in India, like Reliance Industries, are adding synthetic biology to their capabilities, indicating that significant market players in India find this an area worth pursuing. Also, the Indian government has launched

two initiatives, National Biofuels Policy and the National Biopharma Mission, to promote the use of synthetic biology in India.

Figure 3: Creation of the world's first synthetic life form using synthetic biology



SOURCE: INCRED RESEARCH, COMPANY REPORTS

Synthetic Biology (SynBio) in pharmaceuticals

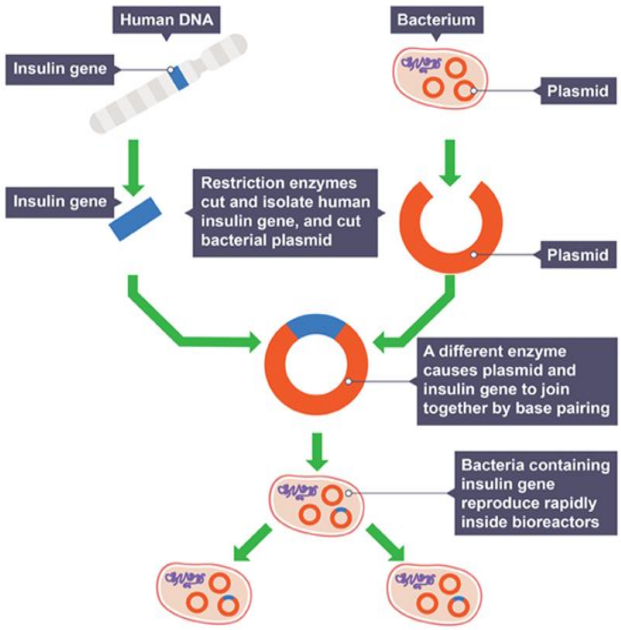
- The SynBio field has developed significantly, paving the way for growth and new opportunities in the pharmaceutical industry.
- It has revolutionized drug discovery by speeding up the identification of new drug targets and high-throughput technologies.
- The synthetic biology toolbox has contributed significantly to developing CAR-T cell immunotherapy. CAR T-cell therapy is a type of immunotherapy that uses a patient's own T cells to fight cancer.
- There has been a sharp rise in start-ups aiming to use SynBio for precision medicine.
- Big pharma, academia, and start-ups are putting in tremendous efforts to use this technology for developing therapies for cancer, rare diseases, and infectious diseases.
- Companies are also exploring using SynBio for biomanufacturing to reduce costs and increase efficiency.

Insulin was one of the first drugs developed using synthetic biology ➤

1. Insulin is a hormone that is made by the pancreas. It breaks down the food we consume into glucose, which provides our body energy. Along with this, it also controls our blood sugar level. Individuals with diabetes cannot utilize or produce insulin properly; hence, they have high blood sugar level, leading to several complications like strokes, blindness, etc. They must be prescribed human-made insulin administered via a pump, injection, or injectable pen.
2. Diabetes was a fatal disease before the discovery of insulin in the early 1900s. Until 1978, it took 8,000 pounds of pancreas glands from 23,500 animals to make one pound of insulin. This method needed to be more efficient to meet the demand for insulin. This motivated Genentech to develop a more efficient means of producing insulin using the newly developed recombinant DNA technology to make each bacterial cell produce insulin in sufficient quantities for the product to be commercially viable.
3. The efforts of Genentech scientists came to fruition in 1982 when the product was approved by the Food and Drug Administration (FDA) and commercialized in 1983. Since then, this drug has changed millions of lives and replaced animal insulin. This is one of the first commercial products developed using synthetic biology, which paved the way for many more. The product was widely successful commercially.

4. Insulin is likely to reach an expected market size of US$21.04bn by 2030F and exhibit a CAGR of 1.5% over 2023F-30F. Biocon manufactures several insulin products in India, including Humulin, Insuman, and Lantus. Laurus Bio, a subsidiary of Laurus Labs, makes a product called Rc carboxypeptidase B that is one of the raw materials used to produce insulin.

Figure 4: Engineering bacterial cells to produce insulin



SOURCE: INCRED RESEARCH, COMPANY REPORTS

Chimeric Antigen Receptor (CAR) T-cell therapy for the treatment of cancer ➤

1. T-cells are a part of the human immune system. They have receptors that recognize these antigens and facilitate killing infected cells after binding them.
2. Scientists are now using this ability of T-cells to use the body's immune system to fight cancer. They engineer T-cells to recognize and attack cancerous cells.
3. These engineered T-cells are called CAR-T cells. The CAR stands for chimeric antigen receptor. The chimeric antigen receptor is the engineered synthetic receptor that recognizes and binds the antigen present in the cancer cells. The advantages of this therapy are that it is effective only against cancer cells and can treat cancers that have become resistant to other treatments.
4. Chimeric Antigen Receptor (CAR) T-cell therapy is one of the most significant clinically relevant synthetic biology applications, with a market value of **US$ 2.54bn in 2022.** Abbvie, Amgen, Gilead Sciences, and Bristol Myers Squibb are some of the big global players involved in this space.
5. The first CAR-T cells in India were designed and produced by the Bioscience and Bioengineering department of IIT Mumbai on 4 June 2021.
6. **ImmunoACT and Immuneel** Therapeutics are the two companies trying to commercialize this product in India.
7. Laurus Labs has a 33.86% stake in ImmunoACT. Kiran Mazumdar-Shaw is one of the co-founders of Immuneel Therapeutics. Apollo Hospitals also has a minority stake in the company.
8. Laurus Labs has also collaborated with IIT Kanpur for in-licensing four patents for three gene therapy programs. The company also plans to set up a CGMP and vector manufacturing facility at IIT Kanpur.

Figure 5: Approved CAR T-cell Therapies

BRAND NAME	GENERIC NAME	TARGETED DISEASE
Kymriah™	tisagenlecleucel	Follicular Lymphoma, Diffuse Large B-cell Lymphoma, or Lymphoblastic Leukemia
Yescarta™	axicabtagene ciloleucel	Follicular Lymphoma or Diffuse Large B-cell Lymphoma
Tecartus™	brexucabtagene autoleucel	Mantle Cell Lymphoma or Acute Lymphoblastic Leukemia
Breyanzi®	lisocabtagene maraleucel	Large B-cell Lymphoma
Abecma®	idecabtagene vicleucel	Relapsed or Refractory Multiple Myeloma
Carvykti™	ciltacabtagene autoleucel	Relapsed or Refractory Multiple Myeloma

SOURCE: INCRED RESEARCH, COMPANY REPORTS

Psilocybin, another SynBio product, has wide applications in psychedelics ➤

1. Psilocybin is a derivative of the amino acid, L-tryptophan. The chemical synthesis of amino acid derivatives is complicated because of their structural complexity. Multiple reactions are involved that give low yields, and optimization is required at each step. Due to the reasons mentioned above, biosynthesis of these compounds is preferred.
2. Psilocybin is a psychedelic (*psychedelics are a class of psychoactive substances that produce changes in perception, mood, and cognitive processes*) that is used for the treatment of depression and post-traumatic stress disorder. More than 200 species of fungi naturally produce it. *S. cerevisiae* and *E. coli* have been engineered to produce psilocybin. 1.2 g/L and 0.6 g/L psilocybin can be produced via these engineered strains.
3. **Octraine Bio**, a Danish synthetic biology company, uses low-cost yeast fermentation to produce psilocybin from sugar.
4. Other companies, like the **Vancouver-based Willow Biosciences**, produces cannabinoids using yeast fermentation.
5. The psychedelic drugs market is anticipated to touch a valuation of **US$11.82 bn by 2029F** from US$4.87bn in 2022, registering a **CAGR of 13.49%** over the forecast duration of 2022-29F.
6. Please note that multiple Indian companies make intermediates for psychedelic drugs. Some of the prominent ones are Ami Organics. PI Industries is also trying to get an entry into this market.
7. Neither of the above companies have any expertise in synthetic biology and it is way beyond their current capabilities.

SynBio method has already helped Ginko Bioworks to develop taxidine - a precursor to anti-cancer drug Taxol ➤

1. Paclitaxel (Taxol) is the most prominent cancer drug, which can act against multiple tumours. It was initially extracted from Pacific yew.
2. The production of the compound involves a tedious and inefficient plant cell culture process.
3. Ginkgo Bioworks has engineered an *E. coli* strain that can produce 1g/L of taxol precursor taxadiene.
4. Ginkgo Bioworks is currently working with several pharmaceutical companies to develop and commercialize taxadiene and other bio-based products. To cite an example, the company has partnered with Bristol Myers Squibb to develop a new process for producing paclitaxel from taxadiene.

5. Cipla sells multiple dosages of Paclitaxel injections for ovarian carcinoma, breast carcinoma, advanced non-small cell lung carcinoma, and AIDS-related Kaposi sarcoma.

SynBio has helped develop multiple mRNA vaccines ➤

1. Vaccines are an essential component of public health. They are used to prevent disease occurrence. Vaccines train our bodies to detect and attack pathogens.
2. **There are several types of vaccines, like attenuated, inactive, toxoids, mRNA, viral vector, sub-unit, and conjugate. Synthetic biology techniques have been successfully applied to the Covid-19 vaccines.**
3. Nucleic acid vaccines, especially RNA vaccines, have caught much traction after the Covid-19 pandemic. The basis behind this idea is that the DNA or RNA enters the body and produces the viral protein. This triggers an immune response, and we build an immunity to the virus. Any epitope can be chosen for this purpose, but most vaccines are in the 5- to 12 kb range because bigger nucleic acids are challenging to deliver. The advantage of these vaccines is the time involved. Once the genomic sequence of the virus is obtained, the vaccine can be designed, manufactured, and tested via trials in weeks.
4. DNA vaccines have higher stability than RNA vaccines and produce the antigen for extended periods. However, they have lower immunogenicity, are challenging to deliver into cells, and carry the risk of genome integration. Due to these reasons, they aren't the preferred choice.
5. RNA vaccines can be designed faster than DNA vaccines, are relatively easier to manufacture, and do not pose the risk of genome integration. However, these vaccines are less stable than DNA vaccines and can be degraded by nucleases around us. The second challenge is to get a strong and consistent expression of antigens from these mRNAs.
6. Synthetic biology and biochemical approaches are used to enhance antigen production, increase stability, and decrease the toxicity of mRNA vaccines. The Pfizer-BioNTech and Moderna Covid-19 vaccines are the first mRNA vaccines authorized by the US FDA. Researchers are also exploring the use of mRNA vaccines for other diseases, such as cancer, HIV, tuberculosis, Zika virus and malaria. After the Covid-19 pandemic, the market value of mRNA vaccine companies has increased exponentially, and there has been an increased effort to develop mRNA therapeutics. The World Health Organization or WHO conducted a tech briefing during the Covid-19 pandemic and assessed 120 manufacturers across Asia, Africa, and Latin America to determine who could manufacture the mRNA vaccine. Wockhardt was the only Indian company that exported a sterile pharmaceutical product to the US and had GMP certification by the US Food and Drug Administration (US FDA). Gennova, a subsidiary of Emcure Pharmaceuticals, has just launched India's first and the world's third mRNA vaccine.

Figure 6: The value of biotech companies working on mRNA platforms shot up multifold after the Covid-19 pandemic

SOURCE: INCRED RESEARCH, COMPANY REPORTS

Diagnostics

Phage (it's a virus which kills bacteria)-based diagnostics is getting revolutionized by using the SynBio method ➤

1. Phage diagnostics is a type of diagnostic test that uses phages to detect and identify bacteria. Phage diagnostics are based on the principle that phages are very specific to the bacteria they infect. This means that if a phage is able to infect a particular bacterium, then that bacterium must be present in the sample being tested. Usually, diagnostics of bacterial infections can take 24-48 hours or longer. Synthetic biology has been used to develop platforms to speed up the diagnosis.
2. Bacteriophages are viruses that destroy bacterial cells. They have been genetically modified to make fluoromycobacteriophages. (*fluoromycobacteriophages are a type of bacteriophage, or virus, that infects and kills mycobacterium bacteria. Mycobacterium bacteria are the causative agents of a variety of diseases, including tuberculosis, leprosy, and Buruli ulcer*).
3. The engineered phages are used for phage-based diagnostics to detect pathogens like *Staphylococcus aureus,* Listeria, *E. coli*, and *Bacillus anthracis (anthrax).* The diagnostics platform prepared using them has a relatively shorter detection time.
4. **Testing for tuberculosis:** For instance, culturing tuberculosis takes up to 10 weeks, but it can be done in 48 hours via this method. Two tests for TB diagnostics have been commercialized via this technology, namely, FastPlaque TB and FastPlaque-Response assays. They have a sensitivity of 95% and a specificity of 97%. FastPlaqueTB is sold by Biotec Laboratories , based in Ipswich, UK.
5. **Testing for S. aureus**: *S. aureus* can cause a wide range of infections, from minor skin infections to life-threatening bloodstream infections. Some of the most common infections caused by *S.aureus* include skin infections like boils and cellulitis, bacteraemia, bone infections, endocarditis, pneumonia, and toxic shock syndrome. Methicillin is an antibiotic that is used to treat *S. aureus* infections. However, some strains of *S. aureus* have developed resistance to methicillin over time. Knowing if a patient is infected by methicillin-resistant *S. aureus* (MRSA) or methicillin-susceptible *S. aureus* (MSSA) is essential to treat the infection. KeyPath is an FDA-approved test that can detect *S. aureus* and differentiate between S. aureus (MRSA)/methicillin-susceptible *S. aureus* (MSSA). This new technology can detect *S. aureus* and differentiate MRSA in 5.5 hours, whereas the traditional methods take more than 48 hours. It has a sensitivity of 91.8 % and a specificity of 98.3%.

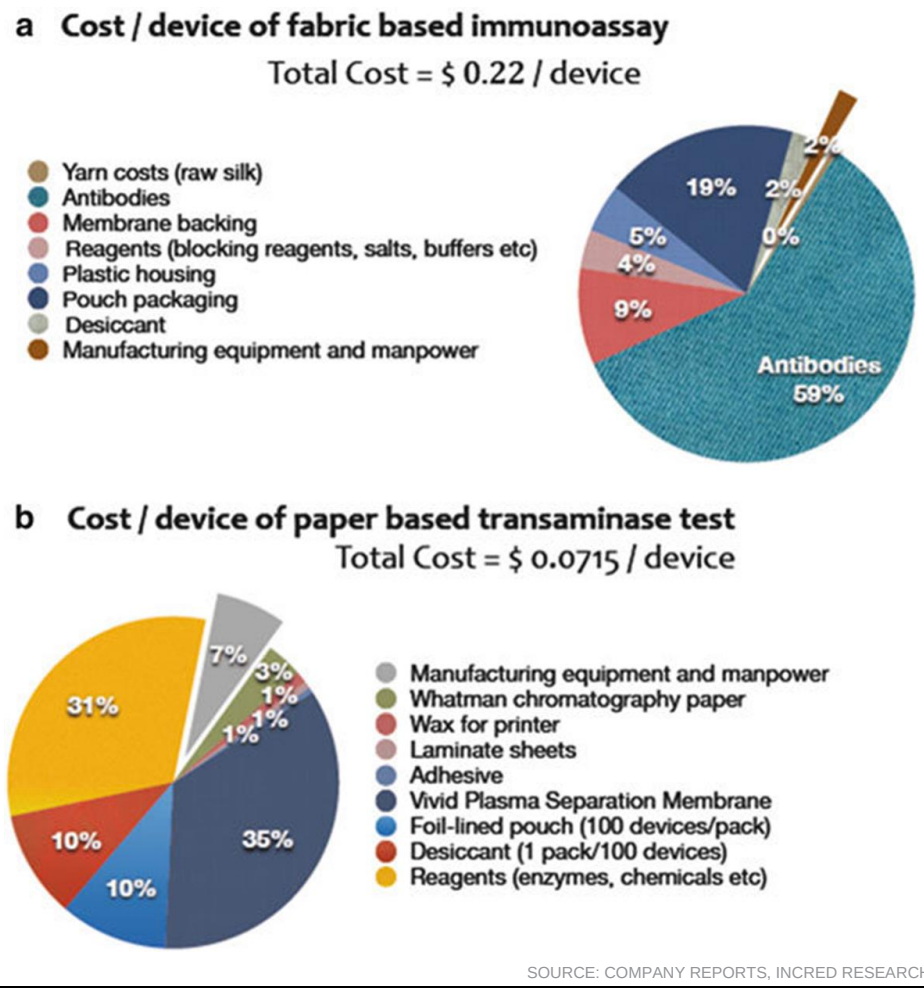
Paper-based testing ➤

1. Scientists have developed a new rapid and cost-effective platform for Zika virus diagnostics. In this, engineered RNAs are frozen on paper and are used to detect the genome of the Zika virus. These paper-based platforms can be stored at room temperature for over a year and reactivated upon adding water.
2. Similarly, other biomolecules like glucose, proteins, or nucleic acids can be applied to paper strips. When samples like blood, urine, or saliva are applied to the paper, the reagent reacts with the biomolecule. It produces a colour change, any other visible reactions detected by the naked eye, or other simple devices like phones. These tests can be used for testing infectious diseases like Covid-19 and non-communicable diseases like diabetes and cancer. Due to their ease of use and stability, these tests benefit areas with limited medical infrastructure. Moreover, they are highly accurate and more cost-friendly than lab-based tests. Overall, paper-based diagnostics meet many of the ASSURED criteria for point-of-care testing, including affordability, sensitivity, specificity, user-friendliness, rapidity, equipment-free, and deliverability.
3. **Boyd Biomedical** has developed paper-based microfluidics devices for point-of-care testing applications. Cipla, a leading Indian pharmaceutical giant, acquired a 21.05% stake in Achira Labs in Jun 2022 for Rs0.25bn. The investment is a part of Cipla's strategy to expand its presence in the point-of-

care diagnostics market.

4. **Achira Labs** is developing a platform called Lab on Paper that uses paper-based diagnostics to provide cost-effective and user-friendly portable diagnostics. The company is developing these tests for thyroid detection, female infertility, and infectious diseases such as malaria, typhoid, and HIV. It is also attempting to use it for diagnosing cancer, heart disease, and diabetes. These platforms are currently in the early stages of development, but they can potentially revolutionize the diagnostics industry in India.

Figure 7: Cost of break-down paper-based immunoassay and transaminase tests being developed by Achira Labs



SOURCE: COMPANY REPORTS, INCRED RESEARCH

Whole-cell biosensor can be used for preventive disease treatment »

Engineered bacterial cells that respond to specific chemicals are whole-cell biosensors. They can be used for disease detection and alerting medical professionals to the early onset of ill health. They are especially useful for detection and monitoring of chronic disorders. Whole-cell biosensors have components like enzymes and cell receptors on them as they are living cells. These allow them to detect different parameters in the body. For example, they can be used to live monitor the effect of a drug on the body.

Chemicals

There is a need for green solutions for the chemical industry, which is one of the most polluting industries. Synthetic biology is the perfect alternative. It is applied in the chemical industry using engineered enzymes or engineered microbes. This technology has already been used to manufacture commodity chemicals like plant-based nylons and specialty chemicals such as fragrances and food additives.

There are various companies active in this field like Genomataica and Solugen ➤

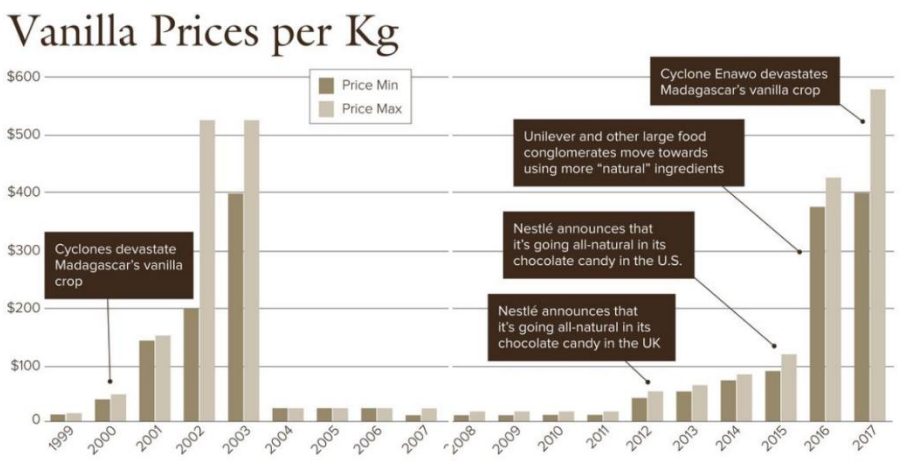
1. The SynBio companies launched in the 90s tried to do an end-to-end process and were not able to succeed commercially. Basically, they focused on a single product only and tried to build all the capabilities required to make the product.
2. Also, many of these companies focused on manufacturing fuel. They couldn't compete with the pricing of the existing players and failed.
3. But some of these companies like **Genomatica** sustained because of their robust technology.
4. The second-generation companies learned from their predecessors and have focused more on platform development, which has given them success.
5. **Solugen is one such company**. Solugen creates enzymes to process the primary input material, corn syrup, into a variety of chemicals, such as hydrogen peroxide and gluconic acid.

Vanillin through the SynBio route ➤

1. Vanillin is a popular flavouring agent used in the fragrance, food, and pharmaceutical industries. Moreover, it is used as a preservative due to its antibacterial, antimutagenic, and antioxidant activities. It is also used in household products like herbicides, floor polish, deodorants, and air fresheners.
2. There is a market demand of 20,000t but only 2,000t is available naturally. Traditionally, vanilla is produced via chemical synthesis and plant-based extraction.
3. It is impossible to meet the demand via plant-based extraction as it costs a lot and has a low yield. Currently, 95% of vanillin is chemically synthesized using lignin and guaiacol as the primary materials. Chemical synthesis has multiple disadvantages, like expensive raw materials, high energy consumption, high pollution, and complex processes. Moreover, petroleum-based vanillin has unsatisfactory aromatic intensity, and the European Expert Committee has imposed restrictions on the amount of synthetic vanillin added to food. Synthetic biology approaches are being used to produce natural vanillin.
4. Evolva produces Everest Vanilla, which is natural vanillin-certified by the USDA's Organic program. This is a sustainable and efficient process that produces better quality vanilla than the conventional practices.
5. The starting material for the process is ferulic acid, a natural produce found in rice bran. A strain of yeast produces vanillin synthase. This enzyme converts ferulic acid to vanillin.
6. Evolva has signed a multi-year agreement with an undisclosed contract manufacturing organization (CMO) partner. Evolva expects to generate a revenue of around US$39m over the next three-and-a-half years from supplying the customer with vanillin as a natural ingredient to the fragrance and flavour industry.
7. Clean Science and Technology makes guaiacol, a precursor for vanillin production. It is the third-largest company in the world and the second-largest in India. If the synthetic biology approaches for vanilla production gain prevalence, Clean Science and Technology will be adversely affected. Camlin

Fine Sciences is producing vanillin using catechol. The introduction of synbio vanillin will affect its revenue too.

Figure 8: Vanilla prices fluctuate a lot and are affected by various natural and global prices; SynBio vanillin will help to stabilize its prices

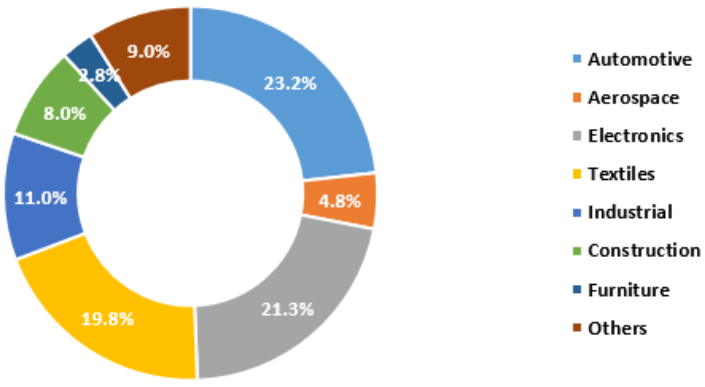


SOURCE: INCRED RESEARCH, COMPANY REPORTS

1,4-butanediol (1,4-BDO) can also be produced through the SynBio route - Genomatica is already doing it ➤

1. 2.5mt of chemicals and polyesters is manufactured annually using 1,4-BDO as a raw material.1,4-BDO is used in a variety of products, including plastics, polyurethane foams, and solvents.
2. It is synthesised primarily using petroleum-based chemical synthesis. However, this method has several disadvantages like non-renewability of raw materials, severe environmental pollution, complicated catalysis conditions and high production cost.
3. Genomatica is a synthetic biology company that is developing a new way to produce 1,4-butanediol (1,4-BDO) using synthetic biology.
4. Genomatica's process uses a genetically engineered strain of *E. coli* to produce 1,4-BDO from renewable feedstocks, such as corn stover or sugarcane bagasse.
5. Genomatica is currently in the process of commercializing its 1,4-BDO production process. The company has a pilot plant in operation and is planning to build a commercial plant soon.

Figure 9: 1,4-BDO finds multiple applications across several industries



SOURCE: INCRED RESEARCH, COMPANY REPORTS

Bio-nylon is another product which is being manufactured through SynBio technology- Genomatica is again the leader ➤

1. Nylon is heavily used in everything, from clothing to packaging. The global nylon industry is worth US$10bn.
2. Crude oil is used as the starting material for nylon production. The molecule, caprolactam, is refined from crude oil and used for nylon production.
3. 5mt of nylon is produced each year, because of which 60mt of greenhouse gases are emitted. Moreover, the production process requires a large amount of energy and water.
4. Genomatica has engineered microorganisms to synthesize caprolactam using sugar as a starting material. Genomatica aims to supply its sustainable nylon to brands like H&M, Vaude, and Carvico through its partnership with Aquafil. Aquafil is one of the biggest producers of nylon globally.

Agriculture

Agriculture accounts for 25% of greenhouse emissions, 70% of freshwater consumption and causes a lot of pollution. We can't possibly meet the total food demand unless we use cutting-edge technologies like synthetic biology, gene engineering, and bioengineering to make agriculture more efficient.

India is one of the leading countries is the agritech space using synthetic biology ➤

Agritech start-up firms in India have raised over Rs66bn (approximately US$900m) in the last four years. Even though synthetic biology in India is still in the nascent phase, it holds tremendous potential for use in the country's agriculture sector.

Multiple global SynBio companies are active in the agriculture space ➤

There is a need for SynBio companies which use this technology to make bio-pesticides and green fertilizers that are more efficient and cause less harm to the environment compared to conventional fertilizers. Below is a table summarizing a few companies working in this space:

Figure 10: Multiple global companies are active in the agritech space

Companies	Technology
Pivot Bio	Nitrogen-fixation
Joyn Bio	Nitrogen-fixation
BioConsortia	Nitrogen-fixation, nematode control, disease control
GreenLight Biosciences	RNA pesticides
Biotalys	Protein-based pesticides

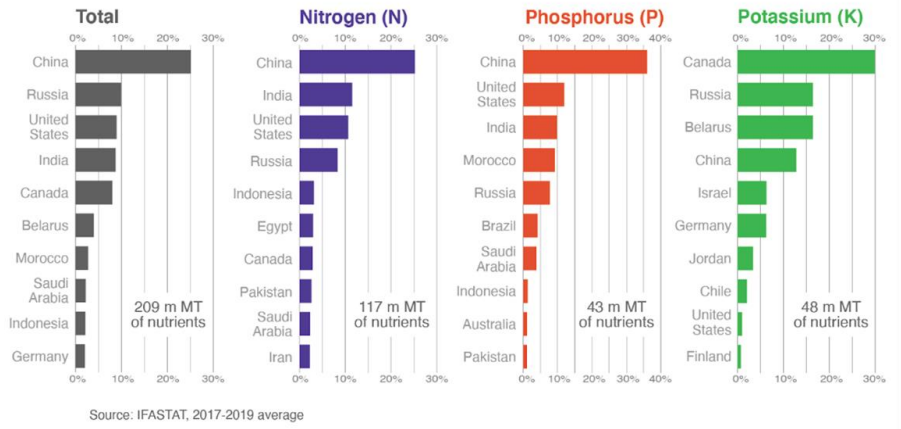
SOURCE: INCRED RESEARCH, COMPANY REPORTS

Nitrogen-fixing bacteria ➤

1. Approximately 140m of nitrogen is synthesized annually utilizing 2% of global energy. Even though it is used as a fertilizer to generate crops that meet the needs of 3.5bn individuals, it does not deliver the required nutrition to the crop efficiently. Approximately 50% of the product is squandered and it emits 1trt (trillion tonne) of CO2 each year, adversely affecting the air quality.
2. PROVEN® 40 by Pivot Bio helps the plant to produce nitrogen and reduce the requirement of synthetic nitrogen fertilizer. It is a fertilizer made up of a bacteria called *Bradyrhizobium japonicum*. The gene for protein leghemoglobin is introduced to the bacteria. The protein helps the bacterium to fix nitrogen from the air. The bacteria attach to the root of the plant and fix the nitrogen, thereby helping the growth of the plant. One of the key advantages of Proven over conventional nitrogen fertilizers is that the entire product reaches the crop, whereas for the synthetic fertilizers the farmers need to over-apply as 40-60% of the product does not reach the crop.
3. Pivot Bio recently shared the results from a study which showed that plants that used Pivot Bio microbes have 14% more nitrogen and 12% more biomass than untreated plants. Based on the 2022 year-end results, Pivot Bio surpassed US$50m in revenue and sold over 3m crop acres, growing three-fold year-on-year. Since the introduction of PROVEN® 40 in 2019, it has replaced synthetic nitrogen on more than 1m crop acres in 2021. This represents more than 300% growth year-on-year and unprecedented agricultural product adoption.
4. Joyn Bio is a collaboration between Ginkgo Bioworks and Bayer. It is engineering a nitrogen-fixing bacteria that could be used instead of nitrogen fertilizer in wheat, corn, and rice crops. Joyn has raised over US$100m from Bayer, Ginkgo, and Viking Global. The product is currently in the development phase. Joyn Bio will license the technology it is making to a seed giant like Bayer or Corteva.
5. India is one of the biggest suppliers and consumers of nitrogen fertilizers globally. While the introduction of products like nitrogen-fixation bacteria will help the agriculture industry it will have a detrimental impact on the fertilizer

industry. Coromandel International gets a sizable revenue from NPK and urea. Some of the other Indian companies that produce nitrogen fertilizers are Chambal Fertilisers and Chemicals, Deepak Fertilizers and Petrochemicals Corporation, Gujarat Narmada Valley Fertilizers & Chemicals (GNFC), and Gujarat State Fertilizers & Chemicals.

Figure 11: India is the second-largest in producing nitrogen fertilizers globally



SOURCE: INCRED RESEARCH, COMPANY REPORTS

Provivi (an US-based company) has tied up with Syngenta to produce pheromone-based insecticides that can replace highly toxic pyrethroids ➤

1. Provivi is an US-based company developing pheromone-based insecticides. Pheromones are naturally occurring chemicals that insects use for communication. Using this technology, the company has developed Provivi FAW, which is effective against the fall armyworm, a pest that attacks over 80 crops, including corn. It comprises two pheromones that disrupt fall armyworm mating by confusing male fall armyworm moths, significantly reducing the next generation of larvae and increasing crop yield.
2. Provivi and Syngenta have launched Nelvium™ through a joint venture in Indonesia. Nelvium is a pheromone-based pesticide detrimental to pests that attacks the rice crop. It is yet again a non-toxic and species-specific solution that utilizes pheromones to disrupt pests' mating behaviour, thereby helping preserve biodiversity.
3. Synthetic biology is used for manufacturing both products. Provivi uses proprietary (bio)catalysts to reduce the steps needed to synthesize pheromones and increase yields. Additionally, Provivi has a multi-year supply agreement for pheromone biomanufacturing with EW Biotech GmbH. EW Biotech is a bioprocess development, scale-up, and contract manufacturing company based in Leuna, Germany. The deal provides critical starting materials for the Provivi FAW™ (fall armyworm) and Pherium™ (rice stem borer) portfolio of products.
4. This product has the potential to replace pyrethroids. In our previous write-ups, we have reported that the pyrethroids market is dying. Pyrethroids harm the environment and human health, and a few pyrethroid products face a ban in certain regions. With the introduction of products which contain insect pheromones that are environment-friendly and have no side effects on human health, the pyrethroids market will be completely wiped out. Herbana has pyrethroids permethrin and cypermethrin in its portfolio.

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