

Plant molecular farming: Industry overview and 2023 developments

Plant molecular farming enables plants to express target molecules, like the animal proteins found in dairy or eggs. Plants can be modified to produce proteins like whey, casein, porcine, or bovine proteins, then are grown at crop-farming scales using well-established farming techniques.

Overview

Molecular farming has long been used in developing pharmaceutical end products like insulin, antibodies, and vaccine antigens. While not a new technology, applying plant molecular farming (PMF) to alternative protein production comes with its own opportunities and challenges.

Since it does not require some of the capital-intensive equipment associated with some other forms of alternative protein production (such as bioreactors), PMF may offer cost and scalability benefits over other production processes. However, as with any novel ingredient solution, the sector will need to successfully navigate regulatory pathways, processing, and purification to establish itself as a viable, scaled technology for alternative protein production. No protein ingredient made in this way has yet been greenlit or approved for commercial sale by a national food safety regulatory body.

This fact sheet summarizes key developments in the PMF sector in 2023.

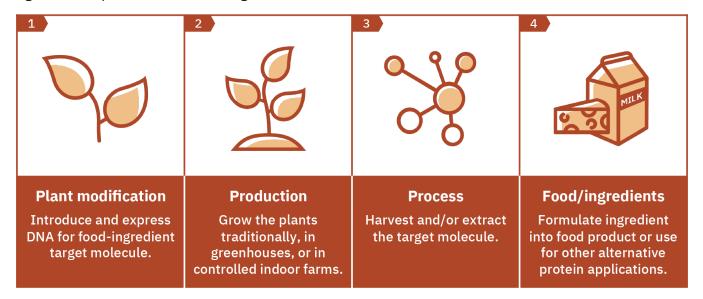


Figure 1: How plant molecular farming works

Commercial landscape

Currently, 15 known companies are primarily focused on advancing this technology for the alternative protein sector. According to GFI's <u>company database</u>, 24 total companies are involved in the space when diversified companies and companies primarily focused on technologies other than PMF are included. There are a variety of product approaches:

- Forte Protein uses plants to produce proteins like lactoferrin, casein, albumen, collagen, and myosin.
- Alpine Bio (formerly Nobell Foods), Miruku, and Mozza produce animal-free dairy proteins for use in products like cheese, ice cream, and yogurt.
- Biobetter, Bright Biotech, ORF Genetics, and Tiamat Sciences create growth factors for cultivated meat media and medicine.
- **PoLoPo** is developing egg proteins.
- Asterix Foods and Imagene are applying the technology toward ingredient optimization for the alternative protein industry.
- IngredientWerks, Kyomei Proteins, and Moolec Science produce bovine and porcine proteins for use in alternative protein products.

2023 developments

Facilities

Israeli food-tech startup **BioBetter** opened a <u>new</u> <u>facility</u> that will use tobacco plants to produce growth factors for cultivated meat.

Partnerships

Two Massachusetts food-tech companies, **IngredientWerks** and **Motif FoodWorks**, announced a <u>partnership</u> to optimize ingredient creation through PMF.

Product development

- **Moolec Science** announced it <u>developed a soy</u> <u>plant</u> able to grow pork protein at an expression level of up to 26.6 percent total soluble protein.
- **IngredientWerks** announced it <u>developed a</u> <u>strain of corn</u> that can express high levels of bovine myoglobin, a heme protein important to the eating experience of beef products.

Nomenclature

As with any emerging industry, the language used to describe plant molecular farming may shift and evolve as the industry grows. For consistency, we refer to this technology as "plant molecular farming" or "PMF" for short, but some companies use different terms to describe their technique and products. For example, **Alpine Bio**, which makes casein using soybeans, describes their process as using "plant-grown proteins," and refers to their final product as "animal-free cheese."

Investments

Table 1: Investments in plant molecular farming(2017-2023)

Year	Invested capital	Deal count
2017	\$25MM	2
2018	\$0MM	Θ
2019	\$3.5MM	2
2020	\$5MM	1
2021	\$106MM	9
2022	\$29MM	10
2023	\$38MM	7
TOTAL	\$206MM	31

Source: GFI analysis of data obtained from Net Zero Insights platform

Plant molecular farming remains a nascent industry with a small number of active companies, meaning industry investment totals can vary significantly from year to year as the result of one or two deals. A GFI analysis of data from Net Zero Insights shows that companies primarily involved in the PMF space raised \$37.8 million in 2023, up from \$29.1 million in 2022 to the second-highest annual total on record. All-time PMF investments surpassed \$200 million.

The vast majority of 2023's investment totals in the sector came from a single fundraising round. **Moolec Science** raised \$30 million in cash and in-kind contributions via convertible notes to ramp up their commercial development plan and product development initiatives, demonstrating one deal's impact on industry-wide fundraising totals. In the coming years, we expect increased involvement from investors as the PMF industry matures.

Liquidity events

Liquidity events represent the sale of an equity owner's interest in a company, typically through a merger, acquisition, buyout, or IPO. In a developing category like PMF, certain liquidity events such as mergers and acquisitions are more common components of industry development. Others, such as IPOs, are less common at this stage. Mergers and acquisitions allow companies with stronger financial footing to acquire firms with valuable technologies, manufacturing processes, and talent. That said, liquidity event activity is also highly dependent on the broader economic context.

One liquidity event, also known as an exit, occurred in 2023: **Moolec Science** <u>acquired</u> Argentina-based **ValoraSoy**, which gave Moolec access to ValoraSoy's soybean processing facilities.

Science and technology

Plants are a compelling platform for recombinant protein production, with years of crop breeding, trait stack development methods, and molecular tools available to produce specific protein products, both recombinant and endogenous.

Further, by harnessing photosynthesis, there is the opportunity to use atmospheric carbon and sunlight (or renewable-powered grow lights) as the principal drivers of ingredient production. Plant molecular farming approaches are an opportunity to produce a variety of alternative proteins using myriad methods, crops, and even plant tissues. Once produced, these specific proteins can be efficiently isolated from plant proteins, or even handled in tandem with bulk plant protein to provide a nutritional or sensory boost to plant proteins. Key opportunities include:

- High-yield, tissue-specific expression of target proteins.
- Inexpensive protein isolation.
- Low-cost inputs (water, light, fertilizers).
- Regulatory pathway clarity.

Advancements across these areas can propel PMF to commercial-scale, low-cost, and sustainable production of proteins capable of elevating the taste and functionality of alternative proteins.

Research across the technology stack

The R&D and scale-up environment for the PMF ecosystem grew in 2023, and progress was reported on a range of alternative proteins. These advances are built on years of progress.

Meat proteins from soybeans

For many companies, soybeans are a compelling development platform for PMF. The soybean plant, Glycine max, is a nodule-forming legume that concentrates nitrogen-fixing bacteria in its roots and produces a high-protein bean. As a major global food system crop, soybean crop breeding and modification strategies are mature, making it a well-studied crop for PMF applications. In 2023, Seedling Biosystems announced they are scaling their first product, a milk protein for the infant formula market, to be produced in soybeans. Moolec Science revealed their Piggy Sooy soybean platform, in which porcine proteins are expressed in soybeans at levels up to 26.6 percent of the protein content and which can then be used as an ingredient in alternative protein products. Kyomei Ltd is using soybeans, among other plants, to express myoglobin proteins for the plant-based meat market, with a stated goal of increasing protein yield for their protein targets.

Dairy proteins from soybeans

Dairy proteins remain a compelling target for alternative protein producers. Improvement of plant-based milk and cheese products with animal-free dairy proteins can provide a "complete protein" containing essential amino acids and high digestible indispensable amino acid scores (DIAAS). Whey proteins can provide important texturization to foods, such as foaming, gelation, and improved mouthfeel. In cheese, casein proteins are complexed with fats and calcium salts in structures called micelles that coagulate to form curds. The functionality of this complex helps make cheese melt and stretch. Mozza Foods has been awarded a <u>U.S. patent</u> for their Cheesebeans[™], soybeans that express casein proteins that can be isolated as micelles and used in animal-free cheese formulations (in a patent-pending process). Alpine Bio has been granted dependent claims to their 2021 U.S. patent, further articulating their technology where proteins, potentially a whey protein (beta-lactoglobulin) and a casein protein (kappa-casein), are expressed as one fusion protein for later downstream processing and formulation. Alpine Bio has applied for additional patent protection on other recombinant fusion proteins in various dicotyledonous plants, demonstrating their focus on novel fusion proteins for use in the alternative protein space.

Alternative proteins from corn

An additional major row crop gets (justifiable) attention in the PMF space. Corn, Zea mays, is planted across more than 80 million acres in the United States, with much of the current crop going to animal feed or biofuel production as a sugar feedstock. Unlocking the agricultural know-how and existing value chain for corn farming and processing could be a major enabling lever for PMF in maize. IngredientWerks, a 2022 spinoff from AgriVida, uses corn to express myoglobin. IngredientWerks plans to isolate the myoglobin from corn for use in alternative protein meat products and return the cornstarch to the value chain where it can be used as a fermentation feedstock. GreenLab has partnered with Gingko Bioworks to develop maize strains and downstream processing approaches to

produce the <u>sweet protein Brazzein from corn</u>. These proteins taste much sweeter than sugar, potentially reducing the need for sugar as a food sweetener. Corn growers also saw a new variety of corn appear on the market—**Bayer Crop Sciences** and **Corteva Agriscience** have unveiled their commercial <u>short-stature corn</u>. This <u>advancement</u> can help eliminate some of the biomass waste from corn stover (stalks, leaves, etc.), which has proven difficult for the agriculture industry to valorize.

Alternative proteins from tobacco plants

Tobacco leaves may not be the first crop to come to mind when one thinks of food; however, *Nicotiana tabacum* is a fast-growing and large-leafed plant, where *Agrobacterium*-mediated gene transfer has enabled smaller-scale <u>recombinant protein</u> <u>production for decades</u>. Israeli-based **BioBetter** has <u>opened a pilot facility</u> to produce recombinant growth factor proteins in tobacco for the cultivated meat industry. This net-house growth facility is built with sustainable engineering designed to minimize water and nitrogen production inputs while lowering the cost of growth factors for the cultivated meat industry.

Elo Life Systems, a **Precision Biosciences** spinoff, announced their <u>monk fruit sweetener derived from</u> <u>*N. tabacum* last year</u>. Unlike sweet proteins like Brazzein or Monelin, monk fruit sweet flavor compounds are triterpene glycoside molecules called mogrosides. Mogrosides are considered zero-calorie and can be used at very low concentrations because they are 100-250x sweeter than sugar. Using PMF to also produce non-protein food products will help to further develop R&D, production technology, and the regulatory space for ingredients made in this way.

Other crops

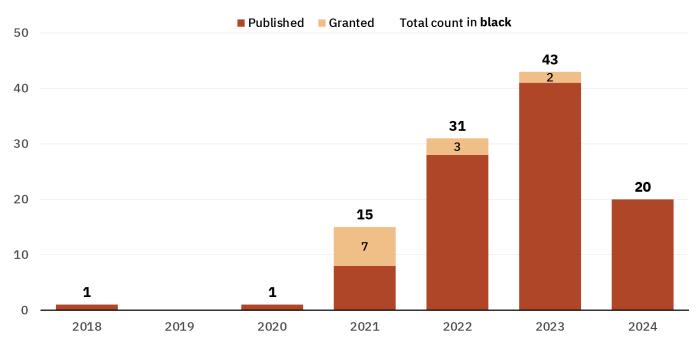
Other crops in addition to soybean, corn, and tobacco can also function well as PMF platforms, and crop breeding and ingredient targets could be co-optimized to reduce the cultivation and downstream processing costs and generate high-yielding functional ingredients. Israel-based **PoLoPo** <u>secured funding</u> to express chicken egg ovalbumin production in potatoes. They plan to launch prototypes soon, including protein-rich potato tubers and ovalbumin functional ingredients. Given potato cultivation's global popularity and chicken egg ovalbumin's in-demand emulsification and gelation functionalities, this system has encouraging potential.

Sustainability

Plant molecular farming can take advantage of indoor production, such as in greenhouse and vertical farms, to avoid the higher regulatory requirements of field-grown crops and to increase the sustainability of plant growth and protein production. **ORF Genetics** grows barley for cultivated meat growth factor production in greenhouses sited to take advantage of Iceland's geothermal power and heat generation, a leading example of renewable energy for the space. The recent attention to vertical farming has led to a push for <u>crop breeding and genetic improvement</u> optimized for the vertical farm environment. Further, both greenhouses and vertical farms could benefit from the valorization of carbon dioxide off-gas and biomass fertilizers produced as sidestreams of the alternative protein industry, which could guide co-location and partnering decisions in the future.

Figure 3: Company focus patent landscape

2018-2023, Q1 2024



Source: GFI analysis of patent data sourced from Dimensions, an inter-linked research information system provided by Digital Science (<u>https://www.dimensions.ai</u>).

The patent landscape includes PMF alternative protein companies included in the GFI company database and this factsheet from 2018 to Q1 2024. Company names and legal filing company names often differ, so these were manually adjusted if available. Duplicate patents were filtered by application number, family ID, and jurisdiction to provide total unique patents across jurisdictions including WO patent applications. Companies searched included Asterix Foods, BioBetter, Bright Biotech, Core Biogenesis, Elo Life Systems, Finally Foods, Forte Protein, Inc., Imagene, IngredientWerks, Kyomei Proteins, Miruku, Moolec Science, Mozza, Nobell Foods, ORF Genetics, and PoLoPo. You can learn more about many of these companies in the <u>GFI company database</u>. Are we missing something? Let us know by filling out our <u>company database edits form</u> or contact us at corporate@gfi.org.

Government and regulation

To date, no protein ingredient made in this way has been greenlit or approved for commercial sale by a national food safety regulatory body. However, in April 2024 Moolec Science achieved a significant regulatory milestone in the U.S. when the Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) completed their Regulatory Status Review (RSR) of the company's new soybean variety that incorporates pork protein, called Piggy Sooy. The RSR determined that Piggy Sooy is unlikely to pose an increased plant pest risk relative to non-engineered soybeans, meaning it will not be subject to a USDA-APHIS regulation that governs the movement of genetically engineered organisms or products. Moolec Science is currently engaged in the U.S. Food and Drug Administration (FDA) consultation process with the goal of bringing their product to market.

Also of note, in 2023 the U.S. FDA Office of Food Safety published an open letter to "Manufacturers and Developers of New Plant Varieties" regarding the production of potentially allergenic proteins within plant platforms. The letter emphasized the need for proper consumer notification of a potential allergen or the combination of plant and recombinant protein allergens. Additionally, the letter calls for special care and consideration for the entire value chain with which the target protein(s) may share equipment, transport, or storage systems. Clear labeling and consumer education of the species of origin and the target protein identity will help to provide consumers with the information that they need to avoid particular allergens. Though focused on pharmaceutical products, a thorough review was published with potential sources of toxicological safety risks from products made via PMF, along with solutions through processing technology, plant breeding, and plant growth environments; all of which demonstrate the awareness of potential hazards for producers and the ability to safely mitigate these risks.

About GFI

The Good Food Institute is a 501(c)(3) nonprofit working internationally to make alternative proteins like plant-based and cultivated meat delicious, affordable, and accessible. GFI advances open-access research, mobilizes resources and talent, and empowers partners across the food system to create a sustainable, secure, and just protein supply. GFI is funded entirely by private philanthropic support.



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