INVENTORY OF SYNTHETIC BIOLOGY PRODUCTS – EXISTING AND POSSIBLE

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Why This Inventory?

For good or ill, new technologies are often defined by a few iconic examples that capture the public imagination. Early on, nanotechnology was defined by its application to stain-resistant clothing and sunscreens, convenient improvements but hardly transformational. Of course, the real revolution was occurring in the background, which involved a newfound ability to see, simulate, and manipulate matter at an atomic scale. Slowly, it became apparent that nanoscale science and engineering were having pervasive impacts across multiple economic sectors and products, as well as up and down value chains, and creating significant potential for improvements in costs and efficiency.

So far, synthetic biology has been associated with a few limited applications, but this initial inventory provides a glimpse of its impact on multiple sectors ranging from energy to pharmaceuticals, chemicals, and food. The real power of synthetic biology may be creating a field of knowledge critical to the design of new technologies and manufacturing processes in general.

This exploratory inventory is an attempt to look over the horizon of this emerging science. As such, it is a "work in progress" and we hope others will help us as we update and expand the inventory. Research on specific applications or near-commercial activities does not guarantee eventual market entry and economic impact, but the breadth of commercial and upstream activity is important to track as the science advances.

Methodology

This inventory of the applications of synthetic biology was compiled from a) a Lexis-Nexis search of US newspapers and newswires on the terms "'synthetic biology' and applications" for the years 2008-2011; b) a Web of Science search on the term "synthetic biology" for 2008-2011; c) a visual search of project descriptions and websites entered into the 2010 and 2011 iGEM competition, as provided on the iGEM website[1]; and d) a web search for specific companies and synthetic biology via Google.

The material from a) and b) was further analyzed by using the data mining and visualization tool QDA Miner[2] with WordStat to select paragraphs that contain one of several keywords and categories which are shown in List A below. The default settings were used. Of the 1,236 newspaper and newswire documents, 1,070 were found to match at least one of the words in the keyword analysis. Of the 397 Web of Science abstracts, 319 were found to match the keyword search.

[1] http://2011.igem.org/Jamboree/Team_Abstracts

[2] See: http://www.provalisresearch.com/QDAMiner/QDAMinerDesc.html

List A: USES

- APPLICATIONS
- BIOFUEL
- CHEMICALS
- CONSERVATION
- COSMETICS
- DRUGS
- ENERGY
- EXPLOSIVES
- FOOD
- FUEL
- MATERIALS
- MEDICINE
- VACCINES

A second data analysis was run on the same data set but included more specific terms related to biofuels, as shown in List B below. This search resulted in 565 of 1,236 news articles and 17 out of 397 matching abstracts from the Web of Science, respectively. The resulting paragraphs containing the keywords were then manually inspected, investigated, and, if appropriate, placed on the list of products and applications.

List B: BIOFUELS

- AUTOMOBILE
- AVIATION
- CAR
- DIESEL
- ETHANOL
- FISCHER-TROPSCH
- GASOLINE
- METHANOL
- PETROLEUM
- PLANE
- REMEDIATION
- FUEL
- TRUCK

The Google web search began with the term "synthetic biology and applications." However, as research continued, other search terms were tried in order to locate potential cases. Some examples include "white biotechnology," "industrial biotechnology," "bioengineered," and "proprietary microbes." "White biotechnology" was much more common in Europe than elsewhere.

The term "synthetic biology" itself was frequently used by small startup companies and in the scientific research literature, while some, in particular large companies (e.g. DSM) with histories of using

genetic engineering techniques, tended to avoid the term. The terms "metabolic engineering" and "systems biology" were not used directly as search terms, though they appeared frequently in results. For some products and processes, determining whether or not they should be classified as "synthetic biology" was a challenge. This is likely a reflection of the uncertainty surrounding the definition of the term. In this analysis, the following definition was applied as a criterion, to the extent possible, given that details of the actual process used are often proprietary:

> *"Synthetic biology is a) the design and construction of new biological parts, devices and systems and b) the re-design of existing natural biological systems for useful purposes."* (Syntheticbiology.org)

Many companies are making precursor chemicals, for example bio-crude oil or succinic acid, that can be refined into any number of fuels or other products. These products often cut across categories. In the product matrix, for chemicals that are being marketed or otherwise intended for multiple uses, the intermediate is listed as a single product. Those listed as "Chemicals" are general chemical products; those that are listed for only one or primarily one use are labeled under that category. Some applications are mentioned under "Other" as they do not fit neatly into the above categories or are flexible enough to be used in many different contexts, such as synthetic multicellular organisms and 'biohybrid' robots. Proofs-of-concept have been demonstrated, and next-step applications are easily imagined in medical, military, and other sectors.

The Market Status of each product is intended to reflect a general qualitative appraisal of where each is in a general product pipeline, or the maturity of the technology, rather than an assessment or prediction of commercial viability. The factors considered were the expressed interest of companies in developing the application, whether funding has been committed, and general progress from laboratory demonstration to actual market availability. The general guidelines for the categories are as follows:

- **Near-term (Green)** = Currently available as product, demonstrations have been running and may be scaled up, seeking out markets and customers
    - **Example:** Amyris' Squalane is available and has received several regulatory approvals
- **Medium-term (Blue)** = Pilot plant built, in clinical trials, joint venture established, holds patents
    - **Example**: Isoprene is currently being pursued by several joint ventures
- **Long-term (Yellow)** = Companies have demonstrated intent to develop this application, but has not progressed beyond small scale or experimental work, applied for patents
    - **Example:** Myriant's Acrylic Acid is under development, but pre-pilot stage
- **On the horizon (Red)** = No commercial development, but some laboratory experimentation
    - **Example:** The process of using yeast to produce terpenes has been demonstrated by one of the iGEM finalist teams, but has not progressed beyond a laboratory setting

Select entries in the inventory include a hyperlink to more information about the products and companies, as well as market status and contact details. These descriptions are based on news reports, company documents, and research papers. Links to sources are also included.

Product Matrix

Category	Product	Organization	Timeframe	Market Status[1]			
				Near-Term	Medium-Term	Long-term	On the Horizon
Biofuel	Algal Biofuels (Bio-oil)	Synthetic Genomics/ExxonMobil	Long-term				
Biofuel	Diesel alternatives (a fatty acid methyl ester (biodiesel ASTM 6751) and an alkane (ASTM D975) from sugar)	LS9 (San Fransico, CA)	Long-term				
Biofuel	Diesel and other "Electrofuels" (Biofuels from Electricity and CO2)	Ginko Bioworks (Boston, MA)	Long-term				
Biofuel	Ethanol from Hybrid Algae	Algenol (Bonita Springs, FL)	Long-term				
Biofuel	Algal Biofuels (Bio-oil) (Green Crude) (Fermentation)	Sapphire Energy (San Diego, CA)	Medium-term				
Biofuel	Butanol	Butamax/DuPont (Wilmington, DE)	Medium-term				
Biofuel	Diesel - Helioculture	Joule Unlimited (Cambridge, MA)	Medium-term				
Biofuel	Ethanol - Cellulosic (Mascoma Grain Technology)	Mascoma	Medium-term				
Biofuel	Algal Biofuels SolaJet, SolaDiesel (bio-oil jet fuel, diesel) (Fermentation)	Solazyme (San Francisco, CA)	Near-term				
Biofuel	Biofuel Feedstock	Chromatin (Chicago, IL)	Near-term				
Biofuel	Biofuel Feedstock - Accellerase TRIO (enzymes for rapid breakdown of cellulose feedstocks)	Genencor (Rochester, NY)	Near-term				
Biofuel	Ethanol - Cellulosic (Process Licenses)	Qteros (Marlborough, MA)	Near-term				
Biofuel	Renewable Diesel and Jet Fuels	Amyris (Emeryville, CA)	Near-term				
Chemicals	D(-) Lactic Acid	Myriant (Quincy, MA)	Near-term				
Chemicals	Isobutanol	Gevo (Englewood, CO)	Near-term				
Chemicals	Squalane	Amyris (Emeryville, CA)	Near-term				
Chemicals	Succinic Acid	BioAmber (Minneapolis, MN)	Near-term				
Chemicals	1,4-butanediol	BioAmber (Minneapolis, MN)	Long-term				
Chemicals	Adipic Acid (nylon precursor)	BioAmber (Minneapolis, MN)	Long-term				
Chemicals	Bio-dispersants (useful for oil spill cleanup)	Modular Genetics, Inc. (Woburn, MA)	Long-term				
Chemicals	butadiene	Genomatica (San Diego, CA)	Long-term				
Chemicals	Fatty Acid, acrylamide	OPX Biotechnologies (Boulder, CO)	Long-term				
Chemicals	Isobutene	Global Bioenergies (Evry, France)	Long-term				
Chemicals	l-Methionine	Metabolic Explorer (Clermont Ferrand, France)	Long-term				
Chemicals	Pomecin B (Anti-fungal)	Evolva (Reinach, Switzerland)	Long-term				
Chemicals	Succinic Acid	DSM (Heerlen, Netherlands)	Long-term				
Chemicals	Sufactants	LS9 (San Fransico, CA)/Proctor & Gamble (Cincinnati, OH)	Long-term				
Chemicals	1,4-butanediol (Bio-BDO)	Genomatica (San Diego, CA)/Tate & Lyle (London, UK)/Novamont (Novara, Italy)	Medium-term				
Chemicals	Adipic Acid (nylon precursor)	Verdezyne (Carlsbad, CA)	Medium-term				

Category	Product	Organization	Timeframe	Market Status[1]			
Chemicals	BioAcrylic	OPX Biotechnologies (Boulder, CO)	Medium-term				
Chemicals	Plasticizers (phtlate free)	BioAmber (Minneapolis, MN)	Medium-term				
Chemicals	Succinic Acid	Myriant (Quincy, MA)	Medium-term				
Chemicals	Sufactants (myristoyl glutamate - used for cleaners, paints, coatings, their version is 10x more effective than conventional versions)	Modular Genetics, Inc. (Woburn, MA)	Medium-term				
Chemicals	1,3-propanediol (Bio-PDO™)	DuPont (Wilmington, DE)/Tate & Lyle (London, UK)/Genecor (Pao Alto, CA)	Near-term				
Chemicals	Biofene (Farnesene) Engineered Yeast	Amyris (Emeryville, CA)	Near-term				
Chemicals	Bacterial "tracking history"	Ginko Bioworks (Boston, MA)	On The Horizon				
Chemicals	H2S sourced fuels and organic compounds	Ginko Bioworks (Boston, MA)	On The Horizon				
Chemicals	Mandelic Acid	Chinese Academy of Sciences	On The Horizon				
Energy	Microbial Fuel Cells efficiency improvement	Nanyang Technological University (Singapore)	On The Horizon				
Food	Vanillin	Evolva (Reinach, Switzerland)	Medium-term				
Food	AnimalFeedProccesing Yeast(MascomaGrain Technology)	Mascoma	Near-term				
Food	Valencene(CitrusFlavoring)	Isobionics (Geleen, Netherlands)/DSM and Allylix (San Diego, CA)	Near-term				
Food	Improvements and modifications to fermentation for food and beverages	Kluyver Centre for Genomics of Industrial Fermentation (Delft, Netherlands)	Long-term				
Food	Stevia (Artificial Sweetner)	Evolva (Reinach, Switzerland)	Long-term				
Food	Sun-driven microbial synthesis of chemicals in space	Harvard/NASA	Long-term				
Materials	Isoprene (Synthetic Rubber precursor)	Goodyear (Akron, OH)/Genencor (Rochester, NY), Amyris (Emeryville, CA)/Michelin (Boulogne-Billancourt, France)	Medium-term				
Materials	PHA (plastics)	Metabolix (Cambridge, MA)	Medium-term				
Materials	Modified polybutylene succinate (mPBS) (Plastic)	BioAmber (Minneapolis, MN)	Near-term				
Medicine	EngineeredInsectStrainsfor population/disease control	Oxitec (Oxford, UK)	Medium-term				
Medicine	AttenuatedVirusCultures for vaccine production	Novartis (Basel, Switzerland)/Synthetic Genomic Vaccines (Rockville, MD)	Medium-term				
Medicine	Antibiotic - Improved processforCephalexin	DSM (Heerlen Netherlands)	Near-term				
Medicine	A1AT deficiency treatment - Intrexon-Alpha 1-Antitrypsin	Intrexon (Blacksburg, VA)/Halozyme (San Diego, CA)	Long-term				
Medicine	Antibiotic - EV-035 (lab testing)	Evolva (Reinach, Switzerland)	Long-term				
Medicine	Arsenic water contamination sensor	Lumin Sensors/iGEM (Team Edinburgh 2006)	Long-Term				

Category	Product	Organization	Timeframe	Market Status[1]			
Medicine	pulmonary arterial hypertension (PAH) therapy	Intrexon (Blacksburg, VA)/Synthetic Genomics (formerly Adeona Pharmaceuticals) (La Jolla, CA)	Long-term				
Medicine	Recombinant Antibodies	Fabrus (La Jolla, CA)	Long-term				
Medicine	CancerTheraputicsZINATI-001 (Ad-RTS-IL-12 + AL)(INXN2001/1001)and ZIN-CTI-001(DC-RTS-IL-12+AL)(INXN3001/1001) atiphaselctiphaselb	ZIOPHARM (New York, NY)/Intrexon (Blacksburg, VA)	Medium-term				
Medicine	Diabetes drug - EV-077 (phase Iia)	Evolva (Reinach, Switzerland)	Medium-term				
Medicine	Artemisinin – Anti-malarial Therapeutic	Amyris (Emeryville, CA)	Near-term				
Medicine	Diabetes drug - Improved manuf process for Sitagliptin	Codexis (Redwood City, CA)/Merck (Darmstadt, Germany)	Near-term				
Medicine	Synthetic lantibiotics	Intrexon (Blacksburg, VA)/Oragenics (Tampa, FL)	On The Horizon				
Medicine	Antibiotics - Nicin variants - New variety of antibiotics (that potentially avoid standard drug resistance)	Carrolll, et. Al. (Cork, Ireland)	On The Horizon				
Medicine	Bacteriophage treatment as antibiotic alternative or supplement	Harvard/BU	On The Horizon				
Medicine	Electrical-Organic interfacing efficiency	Lawrence Berkeley National Laboratory/HHMI	On The Horizon				
Medicine	EnLact probiotics - VT301 for inflammatory bowel disease	ViThera Pharmaceuticals (Cambridge, MA)	Long-term				
Medicine	Using engineered gut bacteria to prevent cholera	Cornell (Ithaca, NY)	On The Horizon				
Other	Tissue-engineered biomimetic jellyfish	Caltech/Harvard	On The Horizon				
Other	Cyberplasm (small swimming robot)	Northeastern University, University of Alabama, MIT and Newcastle University U.K.					

Some representative Projects from the International Genetically Engineered Machines Competition (iGEM)

We include iGEM projects separately as examples of possible future directions for the field. These iGEM projects have been selected on the basis of the following criteria:

- Finalists in the competitions
- Relatively recent
- Have been able to demonstrate a particular real-world application
- Sounded interesting or novel

However, because these are student projects and often thinly resourced, predicting their commercial viability, time to market, and impact is difficult.

More at: http://2012.igem.org/Main_Page

Some representative iGEM Projects

Hyperactive antifreeze protein	Team Yale	Long-term				
Biofilms for photo-lithography	Team Glasgow	On The Horizon				
Cellulose (paper making)	Team TzuChiU Formosa	On The Horizon				
Added vitamins to yeast	Team Johns Hopkins	On The Horizon				
Concrete from regolith (for space exploration)	Team Brown-Stanford	On The Horizon				
Plant Auxin	Team Imperial College London	On The Horizon				
Terpene production in yeast	Team British Columbia	On The Horizon				
Water filtration by E Coli	Team Valencia	On The Horizon				
Energy source from cyanobacteria	Team Brown-Stanford	On The Horizon				
Hyperactive gluten-degrading enzyme	Team Washington	Long-term				

Product Descriptions - Examples

BIOFUELS

Cyanobacteria

What: A patented cyanobacteria seeks to convert carbon dioxide, untreated water and sunlight into liquid hydrocarbons that are the functional equivalent of diesel and ethanol. The company's process, known as Helioculture, does not use biomass feedstock, downstream processing or natural resources and could eventually produce diesel gas at $20-$50 a barrel.

Who: Massachusetts-based Joule is privately held startup founded in 2007 by venture capitalists at Flagship VentureLabs. The company has support from high-profile biologists, including Boston University's James Collins and Harvard University's George Church, as well as political figures like Obama transition team co-chairman John Podesta.

How: The company says its unique, production-ready platform combines breakthroughs in genome engineering, bioprocessing, and hardware engineering to convert sunlight and waste carbon dioxide (CO2) directly into clean, fungible diesel fuel, bypassing the limitations of biofuel production. Joule's production is optimized to facilitate the entire continuous process, scaling up with no dependence on raw materials, agricultural land, fresh water, or crops.

The company plans to use these marginal assets -- abundant sunlight (and warm temperatures), water that is unsuitable for agriculture, under-utilized desert land, and a ready nearby source of CO2 -- to produce up to 25,000 gallons of diesel per acre annually at costs as low as $20 per barrel including subsidies.

In July 2011, Joule received approval for two patents – U.S. Patent #7,981,647 and U.S. Patent #7,968,321 – which cover the enzymatic mechanisms engineered into the cell by the company to help maximize its production of ethanol. The company has six patents overall and 70 pending patent applications. ("Joule Awarded Patents for High Volume Ethanol Production from Sunlight and CO2," http://www.jouleunlimited.com/news/2011/joule-awarded-patents-high-volume-ethanol-production-sunlight-and-co2)

But much like fuels produced from microalgae, there are technical challenges to producing diesel from cyanobacteria. ("As Algae Bloom Fades, Photosynthesis Hopes Still Shine," http://www.nytimes.com/gwire/2011/03/29/29greenwire-as-algae-bloom-fades-photosynthesis-hopes-stil-54180.html?pagewanted=all)

Status: In January 2012, Joule announced that it has raised an additional $70 million in private equity funding, bringing its total capital raised to more than $110 million. The money will fund a test facility in New Mexico, which the company says will be operational by summer 2012. ("Joule Gets $70 Million in Funding for New Mexico Biofuel Plant," http://www.bloomberg.com/news/2012-01-17/joule-gets-70-million-in-funding-for-new-mexico-biofuel-plant.html)

The company has also secured $19 million in state tax incentives for the project after New Mexico's legislature voted to amend the state's Advanced Energy Manufacturing Tax Credit Act to help companies like Joule qualify for the program.

In March 2012, the World Economic Forum (WEF) named Joule as one of its ten emerging technologies for the year. "If it works as planned, Joule will have succeeded in solving three crucial problems facing the world today: producing an affordable fuel of the future, disposing of unwanted waste and finding a profitable use for carbon dioxide, one of the prime suspects in the debate over climate change," WEF says in its report. (Technology Pioneers 2012, http://reports.weforum.org/technology-pioneers-2012/)

Joule says the technology is now proven and working in pilot phase. Commercial production is slated to begin in 2013, according to the company's website.

Economics: According to a February 2012 report from Pike Research, the global biofuels market is expected to double by 2021 to $185.3 billion, up from the current $82.7 billion. The group says the increased production will still fall short of demand. ("Biofuels market to double by 2021 says Pike Research," http://biodiesel-news.com/index.php/2012/02/20/biofuels-market-to-double-by-2021-says-pike-research/)

Liquid biofuels make up "a small but growing contribution" to worldwide fuel usage, according to the Renewable Energy Policy Network for the 21st Century. In 2010, biofuels provided about 2.7 percent of total fuel usage globally, including around 4 percent in the United States and 3 percent in the European Union. In 2010, the United States was the world's largest producer of biofuels, followed by Brazil and the European Union. (Renewables 2011 Global Status Report, http://www.ren21.net/Portals/97/documents/GSR/GSR2011_Master18.pdf)

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CHEMICALS

D(-) Lactic Acid

What: Plastic ingredient D(-) lactic acid can be expensive and costly to produce, but a new process, using renewable, cellulosic feedstock, could reduce the chemical's cost and environmental footprint.

Who: Massachusetts-based Myriant focuses on redeveloping commonly used chemicals to be made from low-cost sugars. In 2011 the company filed for an initial public offering to bring as much as $125 million of capital into the company. The company was spun out of BioEnergy International, also based in Massachusetts. ("Biofuels firm Myriant files for $125M IPO," http://www.masshightech.com/stories/2011/05/30/daily11-Biofuels-firm-Myriant-files-for-125M-IPO.html)

How: While separating D(-) lactic acid and L(+) lactic acid has traditionally required an expensive chemical process, Myriant says its technology "permits the production of D(-) lactic acid alone or L(+) lactic acid alone in one step through biosynthesis—reducing the cost and complexity of the purification process," which allows manufacturers looking to enhance the performance of polylactic acid at a reasonable cost.

Status: Myriant's D(-) lactic acid started production at commercial scale in June 2008 for use in polylactic acid. Meanwhile, the company's succinic acid plant in Lake Providence, Louisiana, is slated to open in 2013; the facility will have a 13,600-ton capacity and use sorghum as a feedstock. ("Myriant Produces Succinic Acid and Lactic Acid From Non-Food Cellulosic Feedstocks," http://www.myriant.com/media/press-releases/myriant-produces-succinic-acid-and-lactic-acid-from-non-food-cellulosic-feedstocks.cfm)

In 2009, Myriant was awarded $50 million by the Department of Energy to help build the Louisiana plant and to bring the succinic acid product to the market. ("Myriant produces succinic and lactic acid from biomass," http://renewablechemicals.agra-net.com/2011/10/myriant-produces-succinic-and-lactic-acid-from-biomass/)

Other products in the company pipeline include acrylic acid for use in diapers and coatings; muconic acid for use in fibers and plastics; and fumaric acid, which is used as a preservative in food and beverages. (Myriant, Product Pipeline, http://www.myriant.com/products/product-pipeline.cfm)

Economics: Citing growing interest in "green chemistry," Myriant says there is a $40 billion market for sustainable chemicals, with the market for succinic acid around $7 billion alone. The company says the lactic acid market is also in the "multi-billion" dollar range. (Myriant Corporate Fact Sheet, http://www.myriant.com/media/press-kit-files/Myriant-CorpFactSheet.pdf)

In a 2011 report, Pike Research estimated that the global green chemistry market would hit $100 billion in 2020. "[M]ost Green Chemicals companies are targeted at large, existing chemical markets, so adoption of these products is limited less by market development issues than by the ability to feed extant markets at required levels of cost and performance," the research firm says. ("Green Chemistry," http://www.pikeresearch.com/research/green-chemistry)

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Isobutanol

What: Isobutanol is a four-carbon alcohol that Gevo is developing from renewable feedstock (rather than petroleum) for the chemicals and fuels markets. The chemical is used in feedstock in the manufacture of isobutyl acetate, which goes into lacquer, paint solvent, and varnish remover. Butanol stores more energy per volume, is less corrosive to pipelines, is more easily separated from water, and can be blended with petrol at higher concentrations than ethanol.

Who: Colorado-based Gevo is a renewable chemicals and advanced biofuels startup developing bio-based alternatives to petroleum-based chemicals. The NASDAQ-listed company was founded in 2005 and its early investors included Khosla Ventures, Virgin Green Fund, Burrill & Co. and Malaysian Life Sciences Capital Fund.

How: Gevo's technology engineers enzymes that can convert waste and other cellulosic feedstocks into alternative fuels like isobutanol and butanol, reducing cost over petroleum-based products. According to press reports, the company plans to deploy the isobutanol using a "capital light" approach, which means existing ethanol-producing facilities can be retrofitted to use the chemicals. ("12 Synthetic Biology Biofuel & Biochemical Companies to Watch," http://greeneconomypost.com/synthetic-biology-biofuel-biochemical-company-17244.htm#ixzz1oeveBFvQ)

Status: The company's commercialization strategy has been focused on isobutanol. The company says the product has cleared the Environmental Protection Agency's (EPA) registration process as a fuel additive and is the first isobutanol to be listed in the EPA's Fuel Registration Directory, which means the chemicals is approved for blending with gasoline. (Isobutanol, http://www.gevo.com/our-business/isobutanol/)

In June 2011, Gevo entered into a joint-venture agreement with South Dakota-based Redfield Energy to retrofit Redfield's existing ethanol plant into an isobutanol plant, which could produce as much as 38 million gallons per year beginning in late 2012.

In May 2012, Gevo announced the startup of the first biomass-fed isobutanol commercial plant, which has a maximum annual production capacity of 18 million gallons per year.

But Gevo is also in a protracted legal battle with Butamax Advanced Biofuels, a joint venture between DuPont and BP, over the patents and processes associated with isobutanol, with Butamax claiming Gevo engaged in patent infringement. (". . . And the biobutanol lawsuit goes on," http://www.icis.com/blogs/green-chemicals/2012/04/and-the-biobutanol-lawsuit-goe.html)

Economics: The global butanol market has mostly been growing in recent years and is expected to reach $9.2 billion in 2015, according to recent filings with the Securities & Exchange Commission. In 2010, the North America and Europe were each responsible for roughly a quarter of the butanol demand; China was responsible for 35 percent of demand. ("Cathay Industrial Biotech files for IPO," http://www.icis.com/blogs/green-chemicals/2011/07/cathay-industrial-biotech-file.html)

Synthetic biology companies producing isobutanol have thus far tended to stay in the chemicals market instead of competing in the cheap fuels market.

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Squalane

What: Neossanse Squalane, along with emollients TMD and HDD, are renewable ingredients for use in cosmetics and personal care products, which are derived using farnesene in a proprietary fermentation process.

Who: California-based Amyris is focused on using sustainable materials, including yeast and plant sugars, to create petroleum-free products like the hydrocarbon farnesene, which can be be used in diesel fuel, as a surfactant used in cleaning products, an ingredient in personal care products, and in industrial lubricants. Founded in 2003, the company first rose to prominence with plans to develop synthetic, affordable artemisinin, an anti-malarial drug. ("How Amyris is Using Green Chemistry to Preserve the Health of Our Oceans," http://www.sustainablebrands.com/news_and_views/nov2011/how-amyris-using-green-chemistry-preserve-health-our-oceans)

How: Farnesene production begins with sugarcane grown in Brazil, which is fermented and uses yeast to convert the sugar feedstock into ethanol. The company engineers the yeast to convert the sugar into isoprenoids, including farnesene, which separates and is recovered from the fermented sugar. The farnesene is then "finished" to be used in a variety of different products. (Production Process, http://www.amyris.com/en/science/production-process)

"Historically, squalane has been primarily sourced either from highly controversial shark liver or from olive oil," Amryis says in a fact sheet on the product. "While olive oil is a more ecofriendly source than shark liver, it is subject to price volatility and limited availability, due to its dual use as a food product." (Neossance Squalane fact sheet, http://www.amyris.com/images/docs/neossance_squalane_datasheet.pdf)

Status: In 2011, Squalane was the first product Amyris brought to the market. In August 2011, the company inked a deal with Nikko Chemicals to supply the product to the Japanese markets. ("Amyris Signs Multi-Year Contract to Supply Renewable Squalane to Nikko Chemicals," http://www.businesswire.com/news/home/20110819005151/en/Amyris-Signs-Multi-Year-Contract-Supply-Renewable-Squalane)

Amyris has contracted to produce farnesene in Brazil, the United States, and Spain to support the commercialization of the product range. The company has also established a chemical-finishing facility in North Carolina and is building two production facilities in Brazil. The Brazilian facilities are expected to be operational in 2012, the company says. (Business Strategy, http://www.amyris.com/index.php?option=com_content&task=view&id=55&Itemid=256)

Economics: Amyris says it is focused on a $67 billion market comprised of five chemical sectors, including a $50-million market for squalane at an average selling price of $30 per kilogram, according to an April 2012 presentation for investors. A 2011 report from Pike Research estimated that the overall global market for "green chemistry" would hit $100 billion in 2020. (April 1, 2012 Investor Presentation, http://files.shareholder.com/downloads/ABEA-4QL2IU/1854655519x0x443773/CA91A4E6-82D9-4A60-BBAF-52251F081CC5/Amyris_Investor_Presentation.pdf)

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Succinic Acid

What: Succinic acid is a dicarboxylic acid used in food and beverages as a sweetener, among other uses, which has traditionally been produced from petroleum-based feedstocks. In addition to food uses, succinic acid is used in drugs, cosmetics, and the production process for numerous chemicals and polymers.

Who: Minneapolis-based BioAmber was founded in 2009 as DNP Green Technology, taking the name BioAmber after a 2010 acquisition. In February 2012, BioAmber completed its Series C round of financing with $30 million from existing investors like Naxos Capital, Sofinnova Partners, Mitsui & Co., and the Cliffton Group, as well as a $10 million investment from specialty chemicals company LANXESS.

How: BioAmber has developed a process to produce succinic acid via bacterial fermentation of glucose, rather than using petroleum-based feedstocks. According to the Environmental Protection Agency (EPA), which awarded BioAmber a "green chemistry" award in 2011, the company "has successfully scaled up an E. coli biocatalyst licensed from the Department of Energy and integrated a novel, water-based downstream purification process," which forms the basis for the fermentation process.

According to EPA, BioAmber is about to produce succinic acid at a cost that is 40 percent less than petroleum-based succinic acid. "Even at oil prices below $40 per barrel, BioAmber's product boasts cost advantages over succinic acid derived from fossil fuels," the agency said at the time of the award. (2011 Small Business Award, http://www.epa.gov/greenchemistry/pubs/pgcc/winners/sba11.html)

EPA says the company has also made it economically feasible to "(1) transform biobased succinic acid into renewable 1,4 butanediol and other four-carbon chemicals; (2) produce succinate esters for use as nontoxic solvents and substitutes for phthalate-based plasticizers in PVC (poly(vinyl chloride) and other polymers; and (3) produce biodegradable, renewable performance plastics."

Status: BioAmber began producing succinic acid in 2010 at a dedicated plant in France and has plans to begin producing the product in North America in 2013. The forthcoming plant, which will be built in Canada, will offer economies of scale and benefit from cheaper feedstock prices, lowering the overall cost of the product, BioAmber says. (Bio-Succinic Acid, http://www.bio-amber.com/bioamber/en/products/succinic_acid)

The company announced plans to file an initial public offering to fund another facility in Thailand and a facility in the United States or Brazil. The company was not profitable in 2011, but started logging revenue from the succinic acid product in early 2012, press reports say. ("BioAmber files for I.P.O. to fund new succinic acid production plants," http://www.ecoseed.org/business-article-list/article/1-business/11848-bioamber-files-for-i-p-o-to-fund-new-succinic-acid-production-plants)

BioAmber and EPA say that the product is the "first direct substitution of a fermentation-derived chemical for a petroleum-derived chemical." The company has also inked partnership agreements with companies like Cargill, DuPont, Mitsubishi Chemical, and Mitsui & Co. (2011 Small Business Award, http://www.epa.gov/greenchemistry/pubs/pgcc/winners/sba11.html)

Economics: As of late 2010, the market for succinic acid is estimated at 40,000 tons per year. Research firm Frost & Sullivan forecasts demand to jump to 180,000 tons per year by 2015, with Bio Amber capturing as much as 50 percent of the market. ("ARD Bio-Based Succinic Acid Plant, France," http://www.chemicals-technology.com/projects/agro-industrie-plant/)

In its IPO filing, Bio Amber estimated a number of markets for its succinic acid: plastics, valued at more than $1 billion; polyurethanes, also valued at more than $1 billion; personal care products, valued at around $500 million; de-icing products, valued at more than $500 million; resins and coatings, valued at more than $500 million; food additives, valued at around 200 million; and lubricants, valued at around $100 million. ("BioAmber's $150 Million IPO: The 10-Minute Version," http://www.biofuelsdigest.com/bdigest/2011/11/15/bioambers-150-million-ipo-the-10-minute-version/)

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MATERIALS

BioAcrylic

What: BioAcrylic is a biochemical product that seeks to replace the petroleum-based acrylic acid current used in myriad consumer products, like paints and adhesive. The substance, if able to be produced at the industrial scale, could potentially cost up to 50 percent less than current acrylic acids and generate a 75 percent reduction in greenhouse gas (GHG) emissions.

Who: OPX Biotechnologies, a Colorado-based company founded in 2007, is using a proprietary technology called Efficiency Directed Genome Engineering, or EDGE, to manufacture bio-based chemicals and fuels that the company says are lower cost and more sustainable than existing petroleum-based products.

How: The firm uses re-engineered microbes to turn renewable feedstock into acrylic acid, which is used in consumer products like paints, diapers and adhesives. According to a 2010 paper from a scientist with the Biotechnology Industry Organization trade group, which cites OPX's work, the key to "realizing these benefits, as with any bio-based product, is a highly productive and efficient microbe able to use renewable sources of carbon and energy (for example corn, sugar cane, or cellulose) in a commercial bioprocess." ("Facts, Growth, and Opportunities in Industrial Biotechnology," http://www.bio.org/articles/facts-growth-and-opportunities-industrial-biotechnology)

In a 2009 presentation at the Symposium on Biotechnology for Fuels and Chemicals, an OPX scientist said that the company is constructing micro-organisms for several bioprocesses, including the bio-refining 3-hydroxypropionic acid, which the company believes will have numerous commercial applications including conversion of the chemical to acrylic acid. ("Rapid optimization of microorganisms for the cost superior production of chemicals and fuels," http://sim.confex.com/sim/31st/techprogram/P10985.HTM)

In February 2011, the company announced the conclusion of a successful pilot that found it possible to make BioAcrylic at a lower cost than petroleum-based acrylic acids. In May 2011, OPX published its patent application for its process for producing 3-hydroxypropionic acid for use in making acrylic acid. ("Production of an Organic Acid and/or Related Chemicals, Application # 12/952,149,"

http://www.google.com/patents/US20110125118?printsec=abstract&dq=opx+biotechnologies+%2B+acrylic+acid&ei=RcJHT_v6FO2w0QHfmJS1Dg#v=onepage&q&f=false)

OPX's EDGE process, used in the production of BioAcrylic, uses a novel, full-genome search technology known as SCALEs, which is up to 5,000 times faster than conventional genetic engineering methods and helps speed up metabolism from years to months. Using EDGE, genes are identified that control microbial metabolism, then a rational genetic change strategy is used to simultaneously optimize microbial production pathways as well as overall bioprocess productivity.

Synthetic biology appears poised to play a role in other new developments in sustainable chemistry. A 2011 book on renewable chemicals and fuels published by the American Chemistry Society (ACS) says that biology will play a large role in the move away from petroleum-based chemicals, citing the OBX work on acrylic acid as an example of the trend. ("The Emergence of Renewable and Sustainable Polymers," http://pubs.acs.org/doi/full/10.1021/bk-2011-1063.ch001)

Status: OPX Biotechnologies has attracted around $41 million in private equity financing. Since 2007, OPX has attracted funding from investors like Altira Group, Braemar Energy Ventures, DBL Investors, Mohr Davidow Ventures, US Renewables Group, Wolfensohn & Company, and X/Seed Capital.

In April 2011, OPX signed a joint development agreement for an 18-month pilot-scale program with Dow Chemical to "prove the technical and economic viability of an industrial-scale process to produce acrylic acid using a fermentable sugar (such as corn and/or cane sugar) feedstock with equal performance qualities as petroleum-based acrylic acid, creating a direct replacement option for the market." If successful, the companies could move to commercial production sometime before 2016. ("Dow and OPXBIO Collaborating on Renewable Route to Acrylic Acid," http://www.opxbio.com/press/Dow_and_OPXBIO_Collaborating_on_Renewable_Route_to_Acrylic_Acid.php)

Current production is about 60,000 pounds per year, anticipated to rise to 600,000 pounds per year by 2013. ("ICIS Green Chemicals: First 2012 post: OPXBio update," http://www.icis.com/blogs/green-chemicals/2012/01/first-2012-post-opxbio-update.html)

OPX is also focused on the biofuels market and working with the National Renewable Energy Laboratory to develop alternatives to petroleum-based fuels. The U.S. Department of Energy's Advanced Research Projects Agency-Energy (ARPA-E) program in September 2011 announced a $6 million award to support OPX's work to use bacteria, electricity, and carbon dioxide to produce a liquid biofuel. ("Biden touts OPX Bio as ARPA-E success story," http://www.biofuelsdigest.com/bdigest/2011/09/05/biden-touts-opx-bio-as-arpa-e-success-story/)

Economics: The petrochemical-based acrylic industry is currently valued at $8 billion and growing at approximately 4 percent per year. While the ACS book on renewable fuels cautioned that "renewable chemicals and materials will not displace petrochemical-based materials overnight," it said on average "the growth rate in renewable chemicals and materials is substantially greater than that for petrochemicals."

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FOOD

Vanillin

What: Biotechnologically produced vanillin provides a vanilla flavor and fragrance for food and other uses without the need to synthesize hydrocarbons derived from fossil sources.

Who: Switzerland-based Evolva is focused on developing synthetic biology products for a number of applications, from biofuels to pharmaceuticals. Established in Switzerland in 2004, the company has opened or acquired facilities in the United States, Denmark, and India. Evolva became a public company in 2009 by merging with Arpida and is listed on the Swiss Stock Exchange. (2009 Annual Report, http://www.aurigapartners.com/download/32_evolva-ar09-en.pdf)

How: Evolva adds genes to yeast to produce new enzymes, which, together with the yeast's own enzymes, will enable the yeast to convert a compound like glucose into the desired product. The company, which has been participating in a 4-year initiative with the Danish Council for Strategic Research, says it has developed an economically feasible and environmentally friendly method of product vanillin via fermentation. Researchers have studied three potential approaches: a genomic approach, a biochemical approach and a proteomic approach. ("De Novo Biosynthesis of Vanillin in Fission Yeast (*Schizosaccharomyces pombe*) and Baker's Yeast (*Saccharomyces cerevisiae*)," http://aem.asm.org/content/75/9/2765.short)

Status: The product is not yet on the market, though the company says it could see full-scale commercial production in 2013 or 2014. Based on the development initiative in Denmark, the company says productions costs have been brought down to a level where vanillin from fermentation will be competitive in some markets. "We are continuing our drive to further increase the process yield while preparing to initiate scale-up by early 2013," the company says on its website. (Vanilla, http://www.evolva.com/nutrition-consumer/vanilla)

Economics: Vanilla and vanillin are important fragrances and food flavorings and together comprise a global market worth $650 million with a total volume of 18,000 tons, according to Evolva. The company says that "only a small fraction" of the total volume is natural vanilla, with the majority consisting of synthetic products. (Vanilla, http://www.evolva.com/nutrition-consumer/vanilla)

In 2010, an expert estimated the synthetic vanilla market to be at 15,000 tons and growing, in particularly noting its increased use as a masking agent. ("Borregaard Ingredients Well Positioned to Meet Global Vanillin Needs," http://www.flex-news-food.com/console/PageViewer.aspx?page=33015)

But some raise concerns that farmers in the developing world could feel the brunt of cheaper synthetic products flowing onto the market. In 2011, Jim Thomas wrote that "Evolva's Vanillin-in-a-vat" could have adverse impacts on the farmers in Madagasgar responsible for the majority of the world's natural vanilla. ("The Sins of Syn Bio: How synthetic biology will bring us cheaper plastics by ruining the poorest nations on Earth,"
http://www.slate.com/articles/technology/future_tense/2011/02/the_sins_of_syn_bio.html)

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Animal Feed Processing

What: Mascoma Grain Technology (MGT) is a genetically modified yeast product that was designed as a "drop-in substitute" for conventional fermenting yeast used in the production of corn ethanol fuel. According to Mascoma Corporation, the maker of MGT, the product lowers production costs for ethanol makers by alleviating the need for expensive enzymes required for ethanol production.

Who: New Hampshire-based Mascoma is a renewable fuels company that focuses on developing new methods for the low-cost conversion of biomass into fuel using its proprietary consolidated bioprocessing technology platform, which includes genetically modified microorganisms to reduce costs and improve yields.

In addition to MGT, Mascoma says it seeks to commercialize other bioprocessing applications. For example, in January 2012 the company said it is "working with collaborators to develop and construct commercial scale facilities to convert hardwood pulpwood to cellulosic ethanol." ("Mascoma Implements Commercialization Strategy for Drop-In MGT Yeast Product to Improve Economics of Corn Ethanol Production," http://www.mascoma.com/download/Mascoma%20_%20MGT%20Press%20Release%20FINAL.pdf)

Investors in the company include General Catalyst Partners, Blackrock, VantagePoint Venture Partners, Kleiner Perkins Caufield & Byers, and others (Our Principal Investors, http://www.mascoma.com/pages/sub_business04.php). The company has received grants from the Michigan Strategic Fund, the province of Alberta, and the Department of Energy. (Our Government Grants, http://www.mascoma.com/pages/sub_business06.php)

How: It has been time-consuming and expensive to develop the necessary system to separate cellulosic sugars from biomass. But Mascoma says with its bioprocessing method it is able to eliminate the separate hydrolysis step and can perform the hydrolysis and fermentation in one consolidated step, thus making the process faster and cheaper. ("I Love You, You're Perfect, Now Scale," http://www.biofuelsdigest.com/bdigest/2011/12/12/i-love-you-youre-perfect-now-scale/)

Status: MGT is the first commercial application of Mascoma's proprietary bioprocessing platform and is now commercially available. The Food & Drug Administration's (FDA) Center for Veterinary Medicine completed its review of the product in 2012 and supports its use to produce animal feed. ("Mascoma gets favorable FDA review of yeast ethanol product," http://www.masshightech.com/stories/2012/02/20/daily30-Mascoma-gets-favorable-FDA-review-of-yeast-ethanol-product.html)

Mascoma and Lallemand Ethanol Technology have both entered into a commercial agreement with Pacific Ethanol for purchases of the MGT product at four ethanol plants with a combined production of about 200 million gallons annually. ("Mascoma and Lallemand Ethanol Technology Announce Commercial Agreement with Pacific Ethanol for Drop-In MGT Yeast Product and Commercial Roll-Out Progress," http://www.businesswire.com/news/home/20120329005708/en/Mascoma-Lallemand-Ethanol-Technology-Announce-Commercial-Agreement)

The company says use of the MGT product can cut enzyme costs by up to 2 cents per gallon, some of which is provided to Mascoma under its agreements with ethanol producers. There are pilot projects under way for future versions of the MGT product, which could improve yields. ("Mascoma garners favorable FDA scientific review on MGT yeast," http://ethanolproducer.com/articles/8603/mascoma-garners-favorable-fda-scientific-review-on-mgt-yeast)

Economics: According to a February 2012 report from Pike Research, the global biofuels market is expected to double by 2021 to $185.3 billion, up from the current $82.7 billion. The group says the increased production will still fall short of demand. The report expects the Americas – lead by the United States and Brazil – to account for around 71 percent of the biofuels produced globally between 2012 and 2021. ("Biofuels market to double by 2021 says Pike Research," http://biodiesel-news.com/index.php/2012/02/20/biofuels-market-to-double-by-2021-says-pike-research/)

The United States produced 49 billion liters of ethanol in 2010 and became a net exporter of the fuel for the first time, exporting 1.3 billion liters, according to the Renewable Energy Policy Network for the 21st Century. (Renewables 2011 Global Status Report, http://www.ren21.net/Portals/97/documents/GSR/GSR2011_Master18.pdf)

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Valencene (Citrus Flavoring)

What: BioValencene is a synthetic bio-based version of the citrus flavor Valencene, which is engineered to give a "juicy impression" when added to food products or fragrances.

Who: Netherlands-based Isobionics Natural Ingredients was established in 2008 and provides products based on natural materials for the flavor and fragrance industries. The company has received funding from Limburg Ventures, Brabant Life Science Seed Fund and others; has a strong relationship with Dutch life sciences and materials company DSM; and collaborates with third-party groups like the Plant Research International Institute at Wageningen Agricultural University. (About Us, http://www.isobionics.com/about_directors.htm)

How: Isobionics uses a controlled fermentation method based on commonly available feedstock to recreate the molecule from the Valencia orange. The process helps create a high-quality molecule that is not dependent on agricultural cycles; saves money by using glucose rather than oranges; and is able to scale up in a shorter timeframe. ("'Unique' fermentation process wins Isobionics an innovation award," http://www.foodnavigator.com/Financial-Industry/Unique-fermentation-process-wins-Isobionics-an-innovation-award)

According to the company, BioValencene has a minimum purity of 75 percent and "the organoleptic characteristics match commercial Valencene qualities available in the market." The produce is kosher and Halal when used in food and considered "natural" in the European Union and United States.

Status: Isobionics began selling BioValencene in June 2010. California-based Allylix has a similar synthetic valencene and says the BioValencene product violates their patents, something Isobionics denies. ("Allylix Sniffs Out Biotech For New Fragrances," http://www.forbes.com/forbes/2010/1108/technology-allylix-fragrances-flavor-carolyn-fritz-smell-test.html)

In 2010, Isobionics' BioValencene won a Frost & Sullivan Global Technology Innovation Award, noting that the company found a way to reduce impurities in the substance while also cutting costs. ("Frost & Sullivan Applauds Isobionics with 2010 Global Technology Innovation Award," http://www.isobionics.com/press3.htm)

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MEDICINE

Engineered Insect Strains for population/disease control

What: Newly engineered versions of insects can be used to help control disease by including a modification that causes their offspring to die or causes male insects to be sterile, reducing insect populations that spread disease.

Who: British biotechnology company Oxitec is a spin-out company from Oxford University and is part of Oxford Spin-out Equity Management, which seeks to maximize the equity stakes of companies borne out of the university. The company has received multiple rounds of financing from Oxford University and private funders, and has received grants from the UK government-funded Biotechnology and Biological Sciences Research Council, World Health Organization and others.

How: Oxitec is developing "RIDL" engineered bugs to help fight dengue fever and reduce damage by insects to crops by developing genetic modifications that make the male insects sterile, though the insects can live normally and reproduce when fed a diet containing a special supplement. The company says the approach is "safe to other species, causes no lasting impact on the environment and is cost-effective." (RIDL Research, http://www.oxitec.com/our-research/)

The company makes a number of products geared towards reducing or eliminating pest insect species, including the *Aedes aegypti* mosquito, pink bollworm and the Mediterranean fruit fly, at a facility in Oxfordshire, United Kingdom.

Oxitec says its Male RIDL insects are released to mate with wild females, but the offspring inherit the engineered RIDL gene and will not survive to adulthood. The Bisex RIDL strains, meanwhile, will allow for no reproduction among the insects unless they are supplied with a diet that includes a special supplement; both male and female progeny die and strains can be designed for termination at different life stages. Female-specific RIDL will have no female progeny unless supplied with the supplement; male progeny will survive. (RIDL Research, http://www.oxitec.com/our-research/)

Status: Oxitec has tested its products in trials in the Cayman Islands and Malaysia. In the open-release Cayman test, company researchers saw an 80 percent reduction in the *Aedes aeqypti* mosquito in less than three months and the insect was not replaced by other disease-carrying species such as *Aedes albopictus*.

The company talked with mosquito abatement officials in Key West, FL, about a similar trail, but plans have been put on hold until a federal regulatory body will oversee the trial. ("Mosquito Control in the Florida Keys," http://blogs.scientificamerican.com/guest-blog/2012/04/11/mosquito-control-in-the-florida-keys/)

According to GeneWatch, which opposes the use of the technology, Oxitec has more than 12 patents for its products. The group raises concerns about Oxitec's business model and the company's relationship with the developing world, among other concerns, in a 2010 report.

"In order for its business model to be viable it will need to lock its customers – presumably developing country governments – into a system of repeated ongoing payments," the group says. "Even if there are no adverse effects, releases of GM mosquitoes will need to be continual to avoid resurgence in the mosquito population." ("Oxitec's genetically-modified mosquitoes: in the public interest?" http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Oxitecbrief_fin.pdf)

Economics: There could be growing demand for systems to stop dengue. Researchers say between 70 million and 100 million cases of dengue virus are reported annually, mostly in tropical and subtropical countries, with around 2.1 million cases of Dengue Hemorrhagic Fever/Dengue Shock Syndrome reported annually. The number of dengue fever epidemics has increased over the last two decades and endemic areas are expanding, research shows.

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Attenuated Virus Cultures for vaccine production

What: The production of vaccines to improve immunity to disease can be increased with the use of a bank of seed viruses, rather than waiting to develop the vaccines based on live reference viruses.

Who: California-based Synthetic Genomics Vaccines, a company formed by Maryland-based Synthetic Genomics and the J. Craig Venter Institute in 2010, is working with Switzerland-based Novartis on a three-year project to develop vaccines based on synthetic genome technology. Synthetic Genomics Vaccines will bring business acumen to the project, while building upon Venter Institute's genomic sequencing and synthetic genomes work, reports say.

The companies are seeking to create a bank of seed viruses to rapidly respond to the annual need for flu and other pandemic vaccines. According to press reports, the collaborative effort is being supported by a grant from the U.S. Biomedical Advanced Research and Development Authority. ("Novartis Teams with Synthetic Genomics Vaccines to Develop Flu Seed Virus Banks," http://www.genengnews.com/gen-news-highlights/novartis-teams-with-synthetic-genomics-vaccines-to-develop-flu-seed-virus-banks/81244037/)

How: The partnership with the pharmaceutical company will seek to cut production time for vaccines by as much as two months by building up the bank of seed viruses, rather than waiting for live reference viruses to be distributed by the World Health Organization. "It has the potential to safely reduce the time needed to develop new vaccines and improve pre-pandemic preparedness," a Novartis research official told *Genetic Engineering & Biotechnology News* in 2010.

Status: In September 2011, Synthetic Genomics Vaccines announced it had hired Dr. Sammy Farah as its president and said the company completed a funding round that "will enable the company to establish operations and support its vaccine programs through initial stages of development." ("Synthetic Genomics Vaccines, Inc. Hires Vaccine Executive Sammy J. Farah as President," http://www.syntheticgenomics.com/media/press/092911.html)

Speaking in April 2012 at Seattle's Institute for Systems Biology, Craig Venter cited the company's work on vaccines as a place for potential use of synthetic biology. "We think we're actually pandemic-ready," Venter said at the event. ("Microbes on the genetic frontier," http://cosmiclog.msnbc.msn.com/_news/2012/04/16/11235389-microbes-on-the-genetic-frontier)

Economics: The worldwide vaccine market continues to grow and is expected to see double-digit growth in the coming years. According to research firm Kalorama Information, global sales of adult vaccines hit $12.5 billion in 2010, an increase of $2 billion over 2009 largely attributed to influenza vaccines. Sales could increase 10 percent per year through 2015, the firm says. Global pediatric vaccines sales are also growing, with 2010 sales at $12.7 billion, up 10 percent from 2009. Pediatric vaccine sales are also estimated to grow, but at a slower rate. ("The Expanding Vaccine Market," http://www.pharmpro.com/articles/201201/business-The-Expanding-Vaccine-Market/)

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Improved process for Cephalexin

What: The antibiotic Cephalexin, which is used to treat infections caused by bacteria such as pneumonia and bone, ear, skin, and urinary tract infections, can be produced in two steps using a metabolic engineering process, rather than some 13 steps using a traditional fermentation process.

Who: Netherlands-based DSM is a life sciences and materials company focused on a number of markets including pharmaceuticals, medical devices, and personal care products, among others. Founded in 1902 as a national mining concern, the company now has around €9 billion in annual sales and its stock trades on the Euronext exchange. (2011 Annual Report, http://www.dsm.com/en_US/cworld/public/investors/pages/publications/annual_report_2011.jsp)

DSM's pharmaceutical arm has five facilities in the United States and Europe providing products to nine of the top 10 pharmaceutical companies, the top three agrochemical companies and a large number of biotech companies, the company says. (DSM Pharmaceutical Products, http://www.dsm.com//en_US/cworld/public/about/pages/dsm_pharmaceutical_products.jsp)

How: DSM's Green Technology uses biocatalyses to produce active pharmaceutical ingredients for antibiotics, including Cephalexin. Rather than a 13-step fermentation process, the company has developed a process with "two enzymatic steps" that use metabolic engineering to produce the ingredients, which reduces emissions, resource and energy consumption, toxicity and risk potential, and area use when compared with the older process. ("Sustainable Production of Pharmaceutical Intermediates and API's," http://www.dsm.com/en_US/downloads/dpp/DSM_Webinar_Sustainable_Production_17Jun09.pdf)

Status: Semisynthetic cephalosporins produced with enzymatic production processes have been on the market since 2000, with companies pointing to multiple benefits for the patients and the environment. ("Sustainability in green pharmaceutical production," http://www.pharmtech.com/pharmtech/Biopharmaceuticals/Sustainability-in-green-pharmaceutical-production/ArticleStandard/Article/detail/574860)

In 2011, the company announced it was launching cephalexin production at a facility in Zibo, China. "The launch in Zibo marks not only the beginning of a new era of purer and safer antibiotic [antibiotic pharmaceutical ingredients] to Chinese finish dosage producers, but is also a unique example of applying green technology in the Chinese pharmaceutical industry," the company said in a press statement. ("DSM Signed Strategic Cooperation Agreement with Guangzhou Baiyunshan on DSM PureActive products," http://www.dsm.com/nl_NL/html/dcn/20091229Agreementwithguangzhoubaiyunshan.htm)

Economics: The antibiotics market is growing, but the growth is slowing. The worldwide antibiotics marked logged $42 billion in sales in 2009, which is 46 percent of sales of all anti-infective agents (including antiviral drugs and vaccines) and 5 percent of the overall pharmaceutical market, according to a 2010 piece in *Nature*. But the journal said the market is "maturing" as the growth rate has slowed over the past five years. ("The Antibiotics Market," http://www.nature.com/nrd/journal/v9/n9/full/nrd3267.html)

In its 2012 Factbook, DSM puts the worldwide anti-infective market at $50 billion in 2010. The company says overall market growth between 2009 and 2013 for its semisynthetic cephalosporins is 3 percent to 5 percent. (DSM Factbook 2012, http://www.dsm.com/en_US/cworld/public/investors/downloads/publications/factbook_2012.pdf)

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Palifosfamide

What: Palifosfamide, also known by the pharmaceutical name Zymafos or ZIO-201, is an experimental drug that seeks to treat metastatic soft-tissue sarcoma, a cancer that forms in in the body's soft tissues and impacts the legs, arms, and abdomen. The maker says the drug is a "novel DNA cross-linker" in a class with other cancer-fighting agents like bendamustine, ifosfamide, and cyclophosphamide.

Who: Ziopharm Oncology, a biopharmaceutical company focused on small molecule and synthetic biology approaches to new cancer therapies, "seeks to develop and commercialize a diverse portfolio of cancer drugs that can address unmet medical needs," according to company financial filings. In addition to palifosfamide, the company is working to develop an "oral tubulin binding agent" to target mitosis and cancer cell migration and an organic arsenic to treat various hematologic and solid cancers.

How: Ziopharm seeks to use DNA as a "pharmaceutical agent" to treat disease, particularly cancer. The company believes DNA can be used to supplement or alter genes within an individual's cells as a therapy to treat disease. Palifosfamide is the functional active metabolite of ifosfamide, which has been shown to be effective in treating testicular cancer, sarcoma and lymphoma, but ifosfamide metabolites include acrolein and chloroacetaldehyde, which are both highly toxic.

According to Ziopharm, preclinical studies have shown palifosfamide has activity in leukemia and solid tumor cancers. "These studies also indicate that palifosfamide has a better safety profile than ifosfamide," most likely because the drug does not include acrolein and chloroacetaldehyde, the company said in 2009. "We believe the administration of palifosfamide may avoid many of the toxicities of ifosfamide without compromising the activity of the drug." ("Clinical Information – Palifosfamide," http://www.ziopharm.com/clinical_zio201.php)

The company says the drug could be beneficial for cancer patients suffering from advanced soft-tissue sarcoma, which is incurable and has a short survival window. An oft-prescribed treatment course of chemotherapy can have severe side effects and reduce quality of life. "In other words this is a difficult problem for the majority of these patients, and a less toxic, hopefully more effective treatment would be hugely beneficial," according to a 2009 paper. ("Palifosfamide - A Novel Molecule for the Treatment of Soft Tissue Sarcoma (STS): A Primer," http://sarcomahelp.org/learning_center/palifosfamide.html)

Status: In 2007, Ziopharm garnered "Orphan Drug" status for the drug from the Food & Drug Administration (FDA), which allows the firm to have seven years of exclusivity for the drug if it reaches the market, among other benefits, in exchange for developing a drug with a limited market. ("What's Next for Ziopharm and Its Cancer Drug?" http://www.minyanville.com/businessmarkets/articles/ziopharm-zymafos-oncology-treatment-drug-american/6/23/2010/id/28893)

In February 2012, the FDA accepted Ziopharm's investigational new drug (IND) application for an oral dose of palifosfamide, which the company says could lead to great development opportunities for the drug. ("ZIOPHARM Announces FDA Acceptance of IND for Oral Palifosfamide," http://www.globenewswire.com/newsroom/news.html?d=244844)

The company says an intravenous form of the drug is currently undergoing a randomized, double-blinded, placebo-controlled Phase 3 trial for the treatment of metastatic soft tissue sarcoma in the front-line setting, called PICASSO 3, and is also completing a Phase 1 study in solid tumors, including small cell lung cancer. The drug is further entering into an adaptive Phase 3 trial in extensive SCLC, which is slated to begin in the second half of 2012. Clinical oral studies are slated to follow.

Economics: The National Cancer Institute says around 9,500 new cases of soft-tissue sarcoma were diagnosed in the United States in 2006, which is less than 1 percent of all new cancer cases. Cancer prevalence in the United States overall was 11,958,000 in 2008, according to American Cancer Society statistics.

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