What's in the CRISPR drawer for farming and food?



ost of us have heard of the gene edited <u>non-browning mushroom</u> that passed through USDA review without the regulatory hurdles faced by transgenic (GMO) crops. And you might have heard of the many different gene edited crops in the pipeline or some of the nimble start ups working in this new breeding space. You might not be aware of just how much the new

technology of gene editing is about to revolutionize the improvement of crops over just the next few years.

It seems like a good time for an overview of the companies outside of the Big Four (Big Three? Big Two? Have I missed another merger?) that are working in this space and what they are working on.

Calyxt

Minnesota-based **Calyxt** has a dizzyingly ambitious pipeline of products, with a nearly equal split of consumer and agronomic traits. The core of the portfolio is high oleic acid soybeans, high fiber wheat, reduced gluten wheat, and lower saturated fat canola. Those are likely to be commercialized over the next two years or so. In earlier stages of development are improved protein content soybeans, cold storable potatoes, reduced browning potatoes, late blight resistant potato, drought tolerant soybeans, improved yield soybeans, powdery mildew resistant what, herbicide tolerant wheat, canola, alfalfa, and finally improved quality alfalfa.

Yield 10 Bioscience

Yield 10 Bioscience <u>focuses very tightly</u> on its "Smart Carbon Grid for Crops" with the goal of eliminating "bottlenecks in plant carbon metabolism by harnessing microbial diversity". The goal is to improve carbon conversion efficiency in crops to increase agricultural yield. They have a smaller portfolio of products than the other companies, but their breeding goals are more ambitious, as they are working to vastly increase the metabolic efficiency of C3 plants (canola, soybean, rice, wheat and potato) in converting atmospheric carbon dioxide into plant biomass to match the efficiency of C4 plants (corn, sugar cane).

The company is currently working on <u>camelina</u> and canola. Camelina is an oilseed that's been studied as an alternative crop in Eastern Oregon and elsewhere in the arid West, since it's capable of surviving with minimal irrigation.

However, the crop isn't widely cultivated because it's currently not profitable enough for growers, said Snell. "You need to get the yield up to make it viable."

Yield 10 Bioscience is examining the possibility of "stacking" the trait associated with increased oil content with other genes that improve yield, potentially making camelina more economically attractive, she said.

Yield 10's higher oil content camelina has been cleared by the USDA for commercialization. If the market

price of camelina was viable, it could compete as a biofuel competitor to kerosene-based jet fuel.

Pairwise Plants

Pairwise Plants is a <u>newer company</u> that just received major investment by Monsanto. <u>Pairwise will work exclusively with Monsanto</u> in corn, soybeans, wheat, cotton and canola crops. Under the companies' collaboration and licensing agreement, Monsanto will contribute \$100 million to access and develop Pairwise IP in row crop applications, including an option to commercialize products resulting from the research collaboration.

<u>Kiersten Stead of Monsanto Growth Ventures told AgFunderNews</u> that Pairwise will have the capability to bring gene-editing to crops beyond the row crops that most gene-editing research has focused on to date. "Pairwise will also be working on a variety of specialty crops through collaborations and directly via in-house precision breeding programs," said Stead.

Gene editing is far less developed in specialty crops than in row crops like corn and soy. Stead said that crops outside the broad-acre category, like tree fruit crops and quinoa, are "underbred," and therefore not as efficient as they could be. "They have not had the benefit of the major ag companies putting hundreds of millions of dollars into modern breeding technologies optimizing these crops to help them produce the most calories and nutrition for the least amount of inputs," she explained.

Caribou

Caribou is a company founded by Jennifer Doudna and Emmanuelle Charpentier, the duo of scientists who adapted CRISPr-CAS9 as a gene editing tool, to put that tool to commercial use. They will be working in the ag/seed trait sector, but have not made any projects public and declined comment for this story.

Cibus

Cibus is small company with about 120 employees based in San Diego but with offices in Minneapolis, Winnipeg and Kapelle, Netherlands. Cibus currently has their SU Canola on the market, a canola paired with <u>Draft</u>, a sulfonylurea herbicide produced by the Canadian company Rotam. They have a partnership with Cargill to connect canola farmers to the non-GMO premium.

Cibus is also developing a glyphosate tolerant crop. It is expected to be launched in the United States in 2019 and in Canada a year later. They are shooting for two herbicide tolerant products for rice. Finally, they are developing a potato that is resistant to Phytophthora, the disease responsible for the Great Famine in Ireland)

I spoke with Cibus president and CEO Peter Beetham by phone. Here are the highlights of our interview:

GLP: Are you in the business of producing seeds? Are you producing SU Canola, or are you licensing the

trait to seed companies and breeders?

Beetham: We developed the SU trait ourselves and we've developed over a number of years a program where we've developed elite hybrids that we are selling into both the US and Canada. Primarily, we are a trait development company and this is our first commercial foray as a combined seed and trait company.

GLP: What are the components of your Rapid Trait Development System (RTDS™)?

Beetham: It's system that uses a whole series of tools. We use everything in our toolkit, that includes our core technologies gene repair oligonucleotides, that is, being able to use oligonucleotides to target direct to mutagenesis. So fundamentally the outcomes of RTDSTM are to direct to mutagenesis. We use cell culture. We use molecular biology tools to find mutations. We are also using

Beetham

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Cibus CEO Peter Beetham

more recent tools like nucleases, the equivalent of TALENs and CRISPRs. So, we use a combination of technologies to get to the end product. The key thing is not all gene editing is the same. When people think of gene editing they may think of CRISPRs or TALENs or zinc fingers, but the key in our deployment is that it's a non-transgenic manner. We don't use any steps that would constitute a GMO.

GLP: So, is RTDS[™] a set of proprietary tools? Or is it the way you systematize and routinize the use of the your preferred tools?

Beetham: We've got a number of proprietary tools in our toolbox, but we also have some trade secrets in how we combine them.

GLP: Let's talk about industry partnerships. I've read that you have partnerships with Cargill and Bunge to connect the canola with the non-GMO sector. Or are you just enabling farmers to enter into those programs that Cargill and Bunge have simply by providing first rate non-GMO seed?

Beetham: We co-market with those guys, particularly Cargill. In North America. We have an agreement with them. When we sell SU Canola seed to a farmer, Cargill calls that farmer to say, we'd like to offer you a premium per hundredweight at the end of the season if you bring that grain to to our crushing facility.

We co-market with them, but the contract is between Cargill and the farmer. But the farmer can sell into the commodity market or the premium non-GE market.

GLP: I know Cargill is partnered with the Non-GMO Project. Where have they weighed in on gene-editing?

Beetham: I think the important thing is that gene-editing is not one thing. But for the Non-GMO Project, their thing has been testing, for transgenics and that's what Cargill contracts with them to do.

GLP: The Non-GMO Project is pretty political organization. They are generally pretty anti-modern agriculture. I think they are eventually going to be pressured into taking a position on gene editing. We'll see how that goes, but I expect they will go one way rather than the other.

Beetham: My thinking on this is that consumers are going to demand more understanding and transparency in their products. I think the USDA is reacting to that with their new Bio-engineering labels. And they will be one among many. I like to think that companies like us and Calyx will work with groups to provide information about what benefits our products provide and the processes into the marketplace.

GLP: I think the Non-GMO Project is going to throw you guys under the bus at one point ... You don't need to comment on that. Moving on. When do you expect to get the glyphosate tolerant flax to market?

Beetham: We'll be doing some more field testing this year and the next. Most likely 2021, it could be as early as 2020, but in that time frame. 2020 would only be a very small launch with a main launch in 2021.

GLP: How big is that market in North America? How many acres looks like success for you?

Beetham: I always think about it like this, every flax grower grows canola, though not every canola grower grows flax. It's couple million acres.

GLP: Is the distribution of SU Canola still confined to North Dakota and Montana? Did I see that there was an expansion into Canada?

Beetham: We did a small launch into Canada this year. It took a few years to get into Canada with a new weed control system, so that's been very exciting to us as a company. So we were able to register some hybrids in Canada and we set up the Canadian team. Mainly selling in Manitoba right now. But we are looking to expand that more broadly into Saskatchewan and Alberta. But at the moment we are focused on Manitoba and a small area around Saskatoon.

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GLP: If I understand correctly, the regulatory process in Canada – they regulate on risk rather than method, so was there greater regulatory scrutiny in terms of that seed/herbicide combined weed control system?

Beetham: In Canada, the Canadian Food Inspection Agency (CFIA) has a thing called Plants with Novel Traits (PNT). So anything that has a new characteristic, and they feel like there is a novelty determination it goes through that process. It doesn't matter what method you use to get there, it goes through that process. That's around a two year process. We've been through that process with our SU Canola and one of our partners took a canola with our technology through that as well.

GLP: Is BASF producing an SU Canola or was that a different product?

Beetham: No, we did some work with them for their Clearfield brand on tolerance of a different herbicide.

GLP: What herbicide are you looking to pair with rice?

Beetham: That's not public information, but we are looking at two different modes of action. The way we see the world is that farmers expect weed control packages on a lot of their seed. That's the case for all the major crops. And that allows them to reduce herbicide use. So we see it as an operating system. When you buy a computer, you expect that it comes with an iOS or Windows.

GLP: Is the plan to stack those herbicide tolerance traits?

Beetham: In certain markets we might stack those traits. In others, that might not make sense. We're agnostic when it comes to chemistry. We're not a chemical company. What we'd like to offer farmers is the best solution for their managing of the their weeds.

GLP: What the timeline look like for commercializing the rice and the potato?

Beetham: It's in the 2020 – 21 time frame. The potato is a little longer. We're still developing that, so it's going to be a few years beyond that. The potato seed industry has a longer pipeline. We might be selling, but consumers might not see that for a few more years. That has to do with the virus resistance and seeing that the seeds are certified – and we'll sell to seed producers before that.

GLP: What's the regulatory environment for gene editing look like in the big rice producing countries? Is it still up in the air?

Beetham: It's very optimistic. What's interesting is that there is a huge appetite for the new characteristics and benefits that this new suite of technologies can bring to the marketplace. I think there is a really strong understanding that these products are indistinguishable from what could occur in nature. What could occur in a breeding program that could take a century or decades, could instead take single digit years. There's a strong appetite for that. There's an education ... it's important for the industry to communicate that there are new tools that we can use that are very precise and accurate. When we are talking to potential customers, but also consumers, that really resonates with them.

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