Interview: Strategic collaborations accelerate bringing products to market

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Israeli plant biotechnology company Evogene is bullish on the prospects of its subsidiaries (agrochemical-focused AgPlenus and biologicals-focused Lavie Bio) and is gearing up for a slew of product launches in the next couple of years. Ofer Haviv, the company's CEO and president, touched upon diverse topics such as the firm's strategies and partnerships, and his thoughts on GM crops and precision agriculture in a candid conversation with Akashpratim Mukhopadhyay.

Akashpratim (AM): Evogene seems to be following a dual business model – engaging with a partner for joint product development and developing its own product pipelines. Which strategy does it intend to follow in the long run?

Ofer Haviv (OH): The model that we follow for the agriculture business is to develop products within our subsidiaries. We look for collaborations only when the development of a product reaches a certain level of maturity, or when we have a candidate and can show some evidence in field trials to prospective partners. In the past, we were presenting the basic technology, and then asking our partners to decide what could be derived out of it. Once that was fixed, we started to look for a candidate and conduct early validation, while our partner would undertake the advanced validation and product development. However, now we prefer our subsidiaries to use the technologies, and we decide on the kind of products are to be developed.

AM: Does the company plan to foray into sales and marketing when its products hit the market?

OH: As far as our marketing strategy is concerned, it will depend on which field the product caters to. In cases where the cost of development and regulation can be borne by a mid-sized company, such as our biological portfolio, we will try to reach all the way to the end-use product and even take responsibility for its sales. At the same time, we can talk to distributors and big companies to release the products.

However, for developing agrochemicals or seed traits where significant regulatory costs are involved, there will come a point when we must approach the big players. We introduce them to the specific candidate, and then engage in collaborations to leverage their experience and budget to take the product to the next regulatory phase. In such cases, our partners will be responsible for the commercial aspects and we will receive royalty from the product.

AM: What are your revenue projections over the next 3-5 years for your subsidiaries, Lavie Bio and AgPlenus?

OH: We are yet to disclose the revenue projections for these two businesses. Lavie Bio is expected to launch its first product, a biostimulant for spring wheat, in 2022. The second product, a biofungicide intended to control Botrytis spp in grapes, is expected to launch in 2024. We are looking for a soft launch of the biostimulant product next year and it will be available to a limited number of farmers. There will not be significant revenue immediately, but from 2023, we are anticipating growing revenues from the first product. There is a huge market for formulations to curb Botrytis spp, and the second offering is also expected to perform very well. We are working on validating the efficacy of the biofungicide on

some other crops as well. Following these two launches, we intend to introduce a new product to the market every year.

AgPlenus is already generating revenues through an ongoing R&D collaboration with Corteva. The company hopes to forge another partnership next year to focus on its internal herbicide pipeline. It has a pipeline of molecules that is advancing nicely, and this could lead to a collaboration with a new partner and present significant revenue potential.

AM: What are your target markets?

OH: The focus for our products is North America. The biostimulant will initially be available in the US state of North Dakota, and then, Canada. We are also keen on exploring the European markets. Field trials are conducted in Europe as well as North America, especially the US. Israel is not a major market, but our R&D activities are concentrated there.

AM: Where does Evogene stand in terms of investments?

OH: So far, Evogene has raised $50 million. A significant portion of the proceeds has been allocated to the activities of our subsidiaries. Our board has decided to spin out some of the subsidiaries, allowing us to raise funds through them separately. This could be done through private placements or public offerings.

For instance, Lavie Bio, and our subsidiary, Canonic, which sits between healthcare and agriculture, is in a great position to raise funds from private as well as public rounds. I am hopeful that during next year, at least one of them will announce a fund raising. It could be in the range of tens of millions of dollars to $40 to $50 million. This is the amount of money they need to move to the next phase. In addition, we expect them to get money from product sales and collaborations.

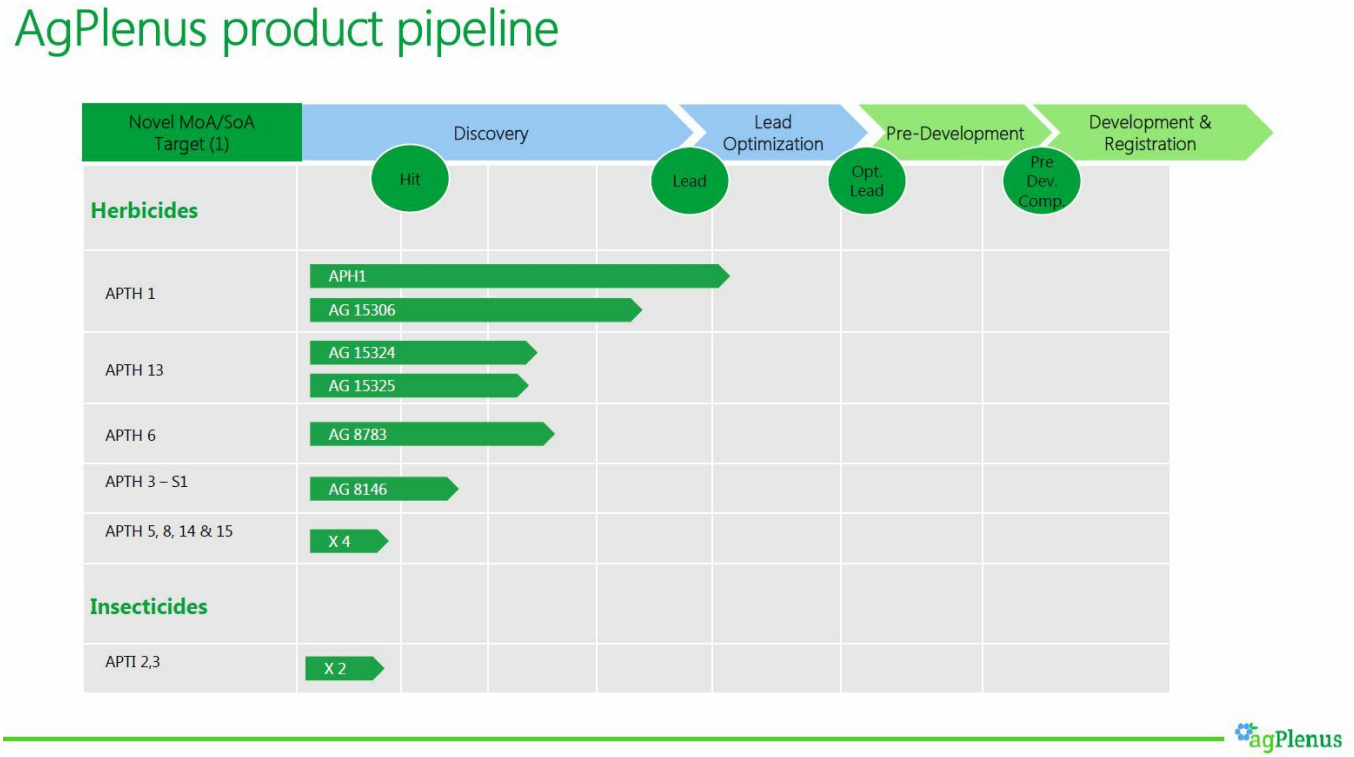
AM: AgPlenus' investor presentations have mentioned leads in herbicides and insecticides. Is there a strategic focus to stay away from fungicides, or is it that fungicidal active ingredients are yet to advance to discovery phase?

OH: The only reason that we have mentioned just the two categories is because of budget and the size of the team. You cannot really do everything. It is not just about discovery, but one also needs to do the validation. For insecticides, we need to build all the infrastructure to grow insects, so that the product can be validated. This is the same with fungicides. For a company the size of AgPlenus, doing everything will be too aggressive. So, they decided to focus mainly on herbicides and insecticides.

Once the company is in a position to raise additional funds, it can expand to fungicides as well. So, it is more a question of focus and financial resources. It is not a technology issue or any other limitation.

AM: AgPlenus recently achieved positive results in a herbicide proof of concept test. Is it a new mode of action and a new chemical class? Could you tell us about the target weeds, especially the resistant weeds that it claims to control?

OH: We are talking about a new mode of action. It is a new protein, and when you stop its activity, the weed is killed. Existing commercial products were not targeting it. If we can block its activity, the crop will not develop resistance to this specific target. This protein should address the problem of weeds resistant to existing offerings. The protein does not exist in mammals, and the safety profile of the product should be pretty high.



Initial validation demonstrated that certain crops have internal resistance to this chemistry. We have also developed a technology that can modify the crop in a way that it will be resistant to the herbicide. This is very important for crops such as soybeans, which do not have resistance to this herbicide. A genetic resistance to the chemistry is needed, so that it can be sprayed during the growing season and act against weeds without harming the crop. We have demonstrated it in tobacco plants and can undertake the same modifications in soybeans. I think the potential of this chemistry is promising and can cover a wide range of crops.

We are targeting as many grass and broadleaf weeds as possible and intend to develop a broad-spectrum herbicide. In practice, as always is the case with proto-herbicides under development, our leading compounds can control part of the weeds from both groups. The issue is the ability to control weeds that are part of the addressed crop and to remain selective to some of them without harming the crop (which we do for maize and wheat).

AM: Your strategic roadmap mentions signing licensing agreements for a new herbicide mode of action (MoA) or insecticide site of action (SoA) in 2021. What has been the progress on that, and could you provide any details of the insecticidal ai?

OH: It will be through collaborations, at least in this stage. AgPlenus does not focus on the regulatory aspect. Its target is to reach the advanced lead stage, after which partners have to take the responsibility for meeting regulations and undertaking commercialisation. AgPlenus will benefit from milestones and the royalty generated through revenues from sales of the product. This business model is different from Lavie Bio, which is focusing on the biological market and reaching all the way to the end-use product, while taking care of regulations.

With regards to AgPlenus' insecticide, we are focusing on a new site of action. While we are still looking at the same protein like in the other commercial product, we are also trying to find another site in the protein that the crop has not developed a resistance to. The solution will mainly focus on insects that are relevant for field crops such as maize and soybeans.

AM: Moving to Lavie Bio, could you provide more details about LAV312 and LAV211? What are the microbial ais in the two products?

OH: We are not looking at the microbes as separate entities. The scientific strategy is to look at genomes as the basic unit.

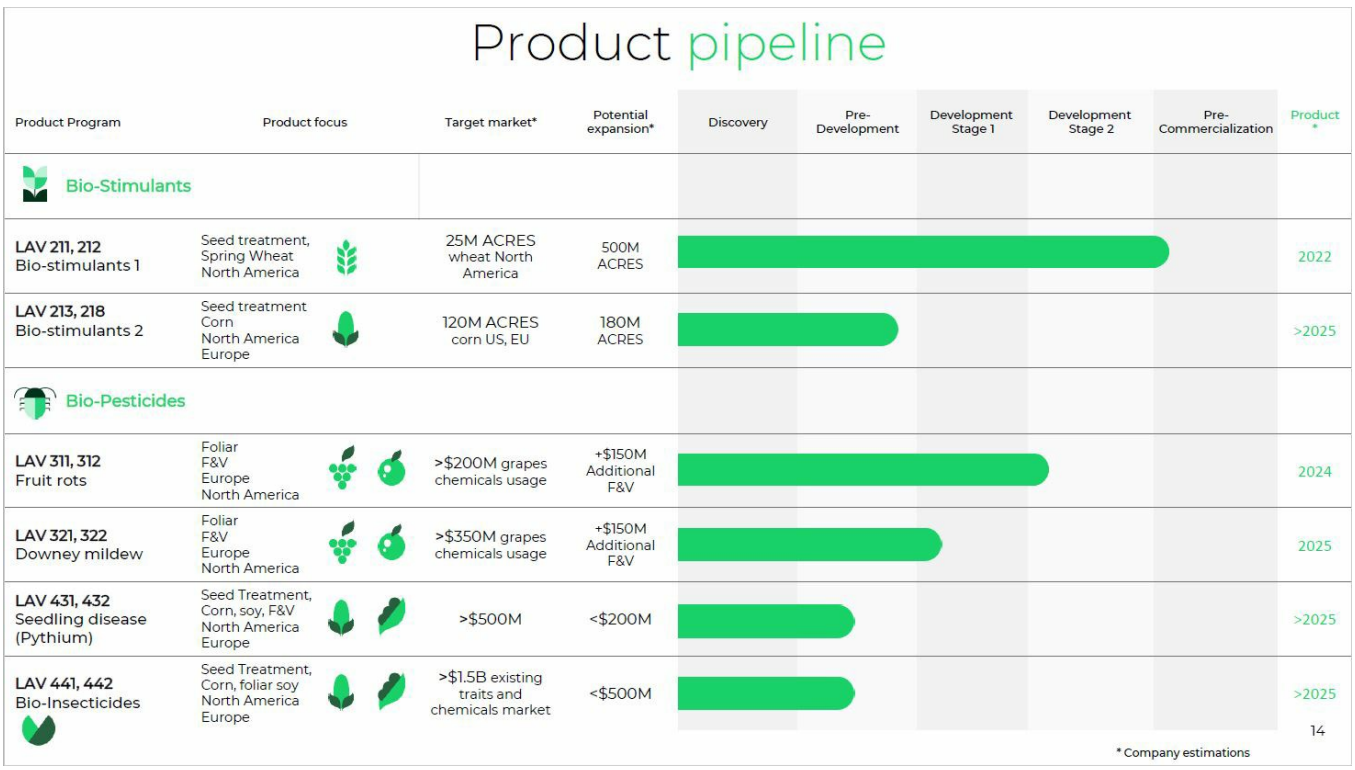
Then, we are analysing which genes can produce the relevant chemistry or metabolites that will achieve the intended effect we are looking for. Once we are clear on what properties the final product should have, we start the discovery phase. Our researchers are looking for microbes with the maximum genomic edge. This translates to finding 2-4 microbes containing the maximum function.

AM: Are plans in place to launch sales of LAV211 in 2022? In which markets globally?

OH: Initially, we are focusing mainly on spring wheat. Our target markets are the US and Canada. This is just the first product that we are validating the microbes on. These microbes improve yield, especially when the crop is facing non-optimal conditions, such as drought or unfavourable weather. Besides yield enhancement, the product boosts overall plant functions during sub-optimal growing conditions.

AM: Where does Lavie Bio stand in terms of its work on biofungicides and bioinsecticides? Are there products in the registration pipeline?

OH: I want to start with the biostimulant. We have already received the approval to start marketing this product in North Dakota. Furthermore, we are planning to initiate the US regulation process for our biofungicide to treat Botrytis spp in grapes. The plan is to complete everything by 2024, when we are planning to launch the product.



The regulation period for biopesticides is longer than for biostimulants. With that on our minds, we will initiate the regulatory process in 2022 and expect it to be over in time for the 2024 launch.

AM: Most biopesticides have been either insecticides or fungicides or nematicides. Do you see a market for bioherbicides?

OH: Yes, certainly. However, the question is, can you find a molecule with efficacy matching that of available chemistries? One of the reasons why people are using biological products is because there is a regulation that forces them to use such formulations instead of chemistries. In the case of herbicides, there is no such regulation in place. So, people will prefer to use something that has proven efficacy.

Companies will start to develop bioherbicides if there are such regulations. This raises another question, are there such

regulators that will put limitations on use of synthetic chemistries, compelling farmers to use bioherbicides. These questions need to be addressed. If they meet with positive responses, we will see companies starting to focus heavily on bioherbicides.

AM: What is the strategic collaboration with Corteva? It owns a stake in Lavie Bio. Are their plans for Corteva to become more involved in AgPlenus as well?

OH: With respect to Lavie Bio, we have a great relationship with Corteva. In addition to working with them on certain programmes and the investment, there is an understanding that they will have some rights to commercialise the product that we are developing, before we start working with other companies. The product that we are developing is suitable for soybeans and maize.

Lavie Bio is very flexible and would work with any other company when it comes to other crops. However, with maize and soybeans, we are obligated to talk with Corteva first. That is not bad at all, because Corteva is leading in maize and soybeans, together with Bayer. The market is divided between these two companies. So, it is not bad to work with Corteva or Bayer in this field. And of course, the terms will be dictated by market conditions.

With respect to AgPlenus, although we have a collaboration with Corteva, they are not shareholders in the company. In the future, we will be more than happy to see them as potential investors. We are yet to discuss this. I feel there is a lot of value in having strategic investors from the shareholder group.

At the same time, we are targeting to bring financial investors to our subsidiaries, because the next step is also to take them to the public market.

AM: Tell us about your pursuits in the GM crop space.

OH: Until 2014, almost all of Evogene's activities were focused on GMO products, and we were also working on new traits. I think the industry cannot ignore that consumers are not in favour of GMO products. Today, the focus is on two traits that have been approved and accepted by the market – insect resistance and herbicide tolerance. In this regard, Evogene is focusing on certain genes that could be a basis for the former category.

The rest of our activity in the area of the genome is very limited. We are waiting to see the market approach with respect to new products. We are interested in genome editing and are a part of the biggest consortium of commercial companies and academic institutions in Israel, CRISPR IL, which focuses on developing genome editing technologies. Evogene is benefiting a lot from this relationship, and we are keen on applying the insights from this partnership to the agriculture sector and explore its different avenues.

However, the business model is not simple, because we assume that this technology will not be considered as GMO technology. This is the state in markets such as the US and Japan. Lately, Japan announced the approval of a GM tomato as a non-GMO product and approved its sales in the country. This is a breakthrough. However, to our sorrow, in Europe, which is a huge market, it seems that genome edited products will be looked at as GMOs, at least for the time being. In our opinion, it is a big mistake.

AM: While Europe has a restrictive outlook on the issue, GM Golden Rice has been cleared for cultivation by the Philippines. Which way do you think the tide is going?

OH: I think the improvement will be very clear in certain cases, such as how such crops contribute to the environment and consumers. Only then, it might change the European opinion about GMOs. I will give an example. If we develop a crop that somehow has a positive effect on climate change, or brings value in stopping global warming, that will be considered in Europe. However, if it is only designed to shore up the revenues of farmers, they will be against it. If the value proposition is for consumers, climate change, and the environment, there will be more acceptance for this technology in Europe.

AM: How does Evogene integrate artificial intelligence (AI) in the CRISPR-Cas platform for genome editing?

OH: One of the areas where we are using AI is to design guided RNAs. Genome editing enables a vector to be directed to

a certain area at the genome, where specific modifications can be undertaken. The problem is that we need something to guide this vector to the specific area in the genome. Finding this specific guide is not so simple. In the CRISPR IL consortium, we are focusing on AI, data and deep learning in order to design the most promising guided RNA, that will take the vector to the specific place in the genome for efficient modification.

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