**Text:** Louise Hagbard, Ph.D. **Photo:** Ola Jacobsen

# STEM CELL INNOVATORS

## KADIMASTEM

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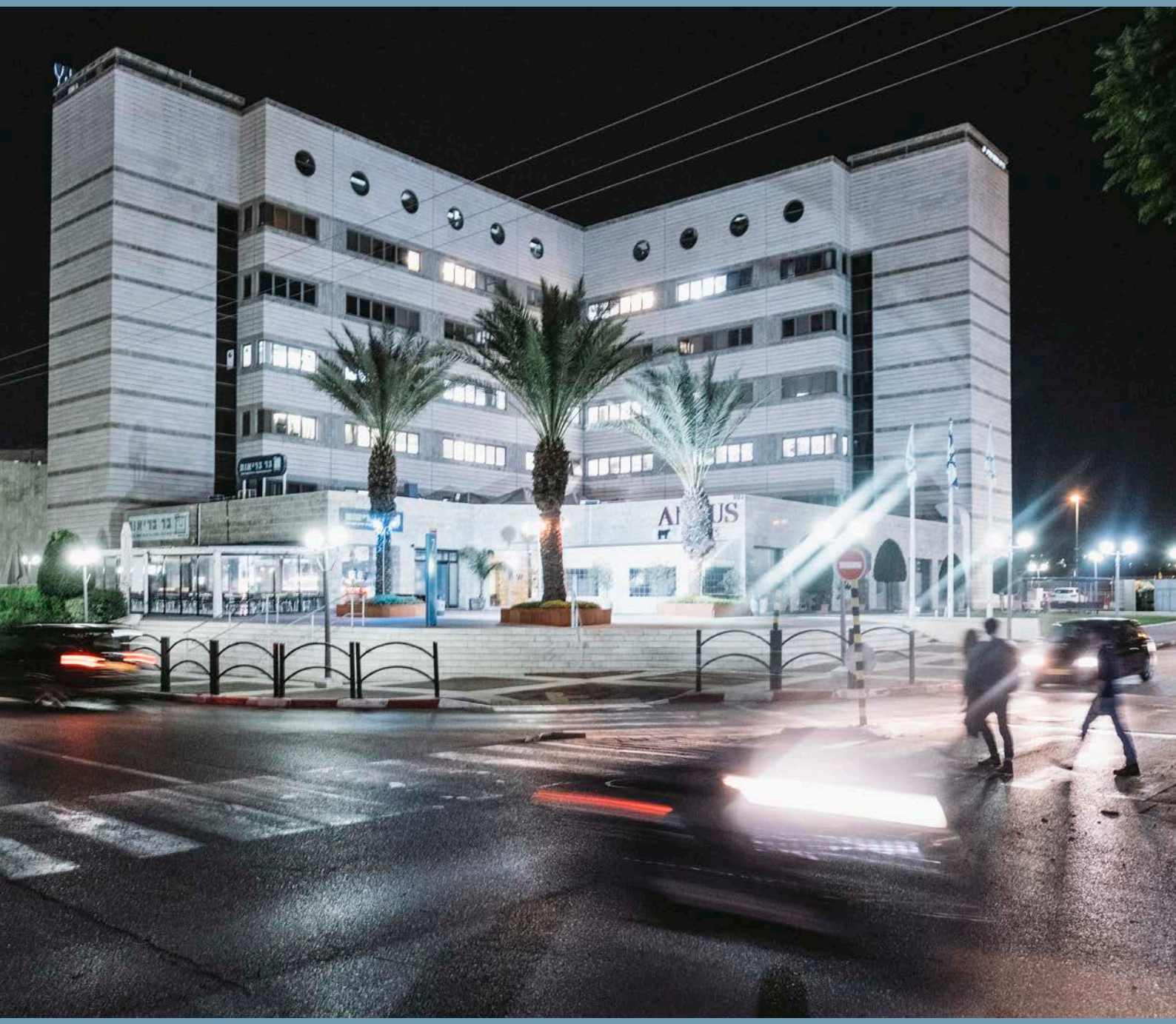

## PEOPLE INTERVIEWED:

ARIK HASSON, Ph.D., EXECUTIVE VP RESEARCH AND DEVELOPMENT

ABOUT: Dr. Hasson holds a Ph.D. in cellular neurobiology from the Hebrew University of Jerusalem and did a post-doctoral research at University of British Columbia in Canada. Dr. Hasson then joined Gamida Cell as head of Stem Cell Projects where he was responsible for the diabetic and neurological projects. As head of Development he helped developing Gamida Cell's first Cell Therapy product, StemEx®, to enter clinical trials. Dr. Hasson helped to initiate the Israeli Consortium for Stem Cells R&D where he served as the R&D Director. Dr. Hasson became Kadimastem 's first employee when it was founded in fall of 2009.

GALIT MAZOOZ, PH.D., DIRECTOR OF BUSINESS DEVELOPMENT

ABOUT: Dr. Mazooz holds a Ph.D. from Weizmann Institute for Science, Rehovot, Israel . She has more than ten years of industrial experience from various positions within R&D and business development. She spent more than five years as senior Licensing Director with focus on Technology Transfer from The Weizmann Institute of Science before joining Kadimastem in 2018.

## KADIMASTEM

Kadimastem, based in Nes-Ziona, Israel, is a clinical stage biopharmaceutical company developing human embryonic stem cell-based regenerative therapies for diseases like diabetes and neurodegenerative diseases, such as ALS. Kadimastem was founded based on patent protected technology, developed by Prof. Michel Revel's laboratory at the Weizmann Institute of Science. The company was founded by in 2009 by Prof. Michel Revel's and Mr. Yossi Ben Yosef, CEO. Kadimastem's astrocyte product, AstroRx, is developed to be used to allow neuroprotection and regenerate and restore survival of the motoneuron cells lost in ALS disease and has started first-in-humans clinical trials at Hadassah Medical Center.

↑ Arik Hasson, Executive VP Research and Development.

**Tell me a bit about Kadimastem's aspirations for the field.**

"We are a clinical stage biopharmaceutical company currently developing human embryonic stem cell-derived therapies for diabetes and ALS," Dr. Hasson, Executive VP Research and Development explains. He continues, "Our diabetes program still has a major focus but since our ALS program has now reached the clinical trial stage, it has become our flagship." It is our chief scientist, Professor Ravel and his team at the Weizmann Institute who has developed a protocol that produce a highly enriched astrocyte cell population. So, the starting material of our astrocyte product are embryonic stem cells, but the final product contains only fully differentiated astrocytes."

Dr. Hasson continues, "I would say that there were two major reasons to why we choose to focus on an ALS therapy. First, we know that astrocytes are central in ALS disease. The function of the astrocytes is to protect and promote survival of nerve cells in the brain and spinal cord. Studies from the late '90s show that the pathogenesis of the ALS disease is caused by malfunctioning astrocytes which results in motor neuron degeneration and paralysis of all the body muscles. There were studies that showed that If you take motor neurons from deceased

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ALS patients or from ALS animal models and add them to a culture of healthy astrocytes, the motor neurons survive. If you do the opposite, not even healthy motor neurons survive. Moreover, there's growing evidence that healthy motor neurons, by themselves, are not enough to support the survival of the ALS patients. So, the astrocytes are important," Dr. Hasson concludes and continues. "The second reason was that we it would be an easier route to the clinic, ALS is a devastating disease and there is currently no treatment. So, we thought that the regulatory authorities would be much more flexible and less problematic in allowing cell therapy trials."

"We have passed extensive efficacy and safety trials and started first clinical trials in humans with our astrocyte product, Dr. Mazooz, Director Of Business Development, adds and continues, "Everything is done here, the research, the development the production and the management. The material for the patient goes directly from here to the hospital."

**Tell me a bit about your research careers and how you ended up here at Kadimastem!**

"I did my Ph.D. at the Weizmann Institute of Science and where I also had a position in tech transfer," Dr. Mazooz explains. "I have been around the industry for many years and have been involved in starting companies here in Israel. I first got in contact with Kadimastem when I was at Weizmann institute so I was on the other side of the table and I was following that process and the company as it grew. After a while, a position at the business development team became available at Kadimastem. That how I ended up here and it has been a great decision for me. Kadimastem is not a large company, about 40 people, and it feel like we are a small family," Dr. Mazooz says and smiles.

Arik nods and continues, "I did my Ph.D. at Hebrew University of Jerusalem and a post-doctoral period at University of British Columbia. I was interested in the stem cell field and I wanted to go to the industry. I got a position at Gamida Cell, a stem cell therapeutic company, where I helped them develop their first Cell Therapy product and to enter clinical trials. I also involved in starting an Israeli stem cell consortium that involved both academia and industry. When Kadimastem was about to be started, I was already in contact with Professor Revel (chief scientist at Kadimastem) and I became the first employee of the company. I was the one that found the

↑ Kadimastem is a clinical stage biopharmaceutical company developing human embryonic stem cell-based regenerative therapies.

## HIGHLIGHTED PUBLICATION

**Safety and efficacy of human embryonic stem cell-derived astrocytes following intrathecal transplantation in SOD1(G93A) and NSG animal models.**
**Izrael M. et al.**
***Stem cell research & therapy, 2018. doi: 10.1186/s13287-018-0890-5***

"We have a mindset towards innovation together with a mentality of survival and we know how to translate and commercialize basic science."

facilities that we are in now. So, we started with only one wing of this building and it was nothing here, totally empty. When the company grew, we moved all the R&D laboratories downstairs and we also had the opportunity to rent another wing which already contained a GMP facility. We had to make investments to upgrade and reorganize the GMP facility but it was a great opportunity and we took it," says Dr. Hasson.

**What do you think has been the biggest hurdles for you during your first ten years as a company?**

"The major hurdle, I think, was conducting the pre-clinical efficacy study which could prove to us that this project was actually worth perusing," says Dr. Hasson. "In addition, we had to do a safety study which was very costly and took a lot of time." Dr. Hasson continues, "If there would have better animal models available, that could have saved us a lot of time and money. I think that is a general problem in drug development, that the animal models are suboptimal. Moreover, we are much more experienced now. It took us about four to five years until we could do our first trial in humans. I think that is quite an OK timespan but I think that if we would do the same project today, it would take us much less time," Dr. Hasson concludes.

"We are a small biotech company and do not have the same economical muscles compared to a similar company in Europe or in the US. To reach the stage where we are in now, they would probably have invested three-four times the money," says Dr. Mazooz. She continues, "We will not be given any short cuts, we have to keep to the standards set by the FDA so we need to be innovative, always trying to find new ways. I think that is one of our strengths and the reason why we have been able to compete with other companies," she concludes. "We should mention that we have had great support by the government. We have invested about $40 million, and about 25% has been governmental support. So, the government, the Innovation Authority of Israel, has put in a substantial amount," says Dr. Mazooz .

"I think that one of the major advantages of working within the biotech field here in Israel is that we have a mindset towards innovation together with a mentality of survival," says Dr. Hasson. "If you are discussing the possibilities of taking a protocol to clinical trials, it will not be a question about why?, it will more be a question about when? That is why there is a lot of clinical trials going on here, especially if you compared it to the economical size of Israel," Dr. Hasson concludes.

"I agree," says Dr. Mazooz, "And one of our strengths is that we know how to take basic science from the academia and translate it to industry". She continues, "I have a lot of experience in taking the basic sciences to make something commercial, and I know it is not easy, but we are good at it and there has actually been a lot of big universities from around the world that has come to Israel, to learn from us how to do it."

**What do you think will be the biggest hurdle to actually make your ALS treatment reach the clinic?**

"We are very happy with our astrocyte protocol and we really believe in our product," Dr. Hasson says and continues, "We are capable of producing the astrocytes in large quantities, billions of cells. We have done the safety studies and are now in the beginning of the secondary step, looking at efficacy. We have started the first-in-human clinical trial at Hadassah Medical Center but it will take us at least a year before we can see the results of the first cohorts but if the read out is similar to those from the animal studies, we may have very nice results.

"The next step will be to develop our AstroRx product so that it can be proliferated and frozen so that we just need to thaw the cells, culture them for few days and then inject into the patients," says Dr. Hasson.

"Ultimately, we want to develop something that is a completely off-the-shelf product. It is complicated though because the current protocols for freezing cells contain DMSO which is toxic for the brain and will not be approved by the regulatory bodies. We hope to complete phase three clinical trials even without completely freezing the cells because the major ALS clinics in the USA or in Europe can be covered by a six-hour travel from a con-

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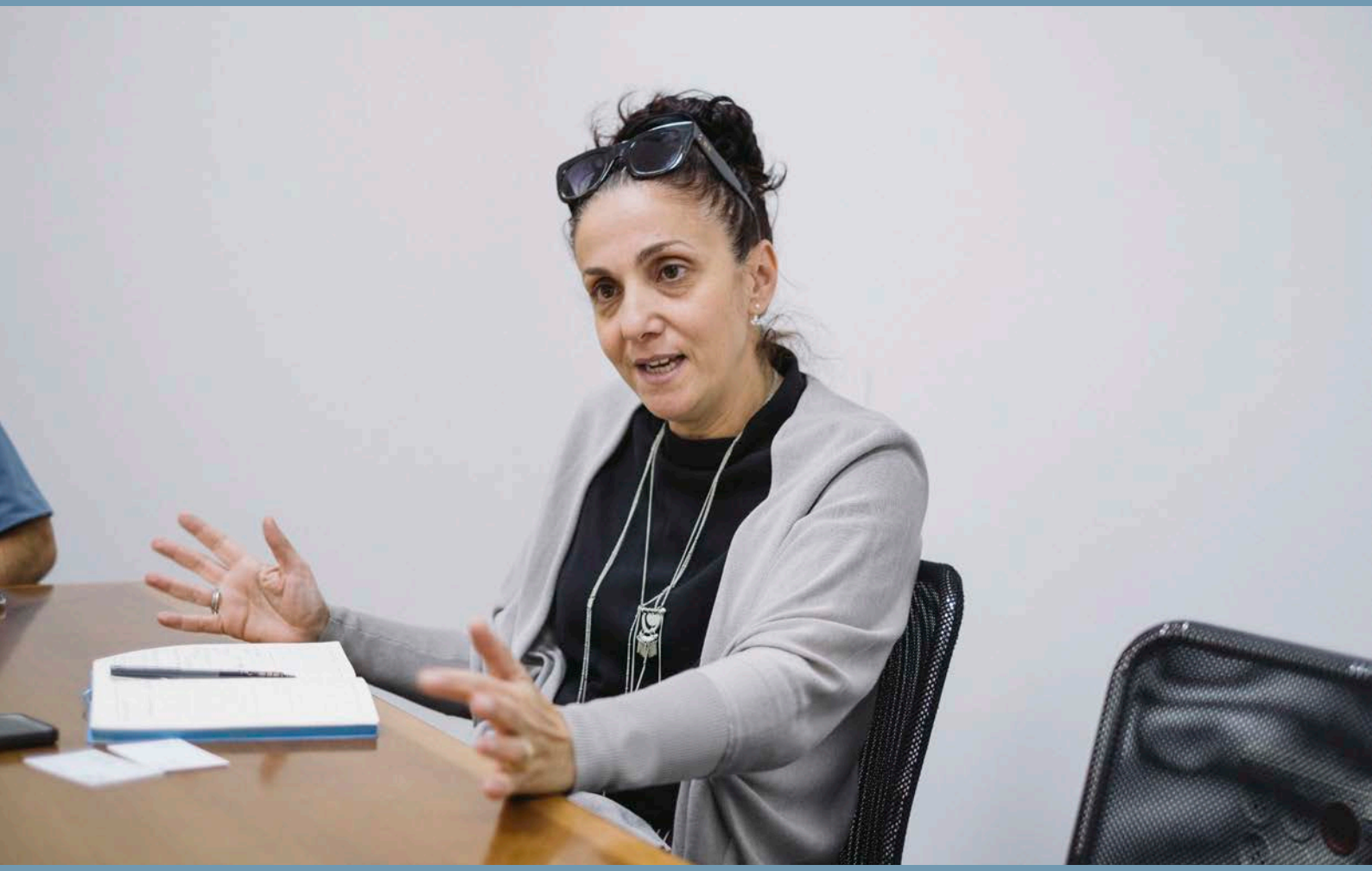
Galit Mazooz, Director Of Business Development.



"If our product works well in ALS patients, we believe that we might be able to use our cells to also treat other neurodegenerative diseases."

tract manufacturing organization and we know that the cells survive well for at least 24 hours," Dr. Hasson says.

**What else do you have in pipeline?**
"Our main focus right now is on the clinical progress of our ALS program. If our product works well in ALS patients, we believe that we might be able to use our cells to also treat other neurodegenerative diseases," says Dr. Hasson.

**What are your thoughts around the used of hESC- vs. iPSC-based protocols for clinical applications?**
"We are also worked a bit with iPS cells and they work equally well as human embryonic stem cells in our differentiation methodologies," says Dr. Hasson. "Why we are mainly using hESCs is because we believe that hESCs are actually the real source material. We have a source of very good human embryonic stem cells and since these cells were formed in a test tube and would be destroyed anyway, we don't see any ethical dilemma either in using these cells. Moreover, there are known problems, like somatic mutations in iPS and we do not want to take that risk," Dr. Hasson explains.

**So, how did you end up in science in the first place?**
"For me, there was no other option," says Dr. Mazooz, "but my firsthand choice was actually to study medicine. I tried to get in to medical school but did not manage. In the end, I had to give up that dream and I chose to study chemistry instead. My father is a chemist, so it was natural to move to follow his step. I studied chemistry but my career has afterwards always had a more biological focus. I have to say, what I am doing today actually comes quite close to my dream of curing diseases, doing something that is for the best of mankind," Dr. Mazooz says and smiles. She continues, "I think science brings something extraordinary to your life. It brings excitement and every day is different. Every day you learn something new. That is exciting!"

"My story is a bit different," says Dr. Hasson. "When I was a kid, I wanted to be a zoology professor in Tel Aviv University, because they had the best zoology department in Israel," says Dr. Hasson. He continues, "Before I went to the university, I spent a couple of years in the Israeli Army and traveled a bit. I had the opportunity to study basically anything I wanted, medicine, phycology or biology. Eventually, I chose to study biology, in Jerusalem not in Tel Aviv. If I would have chosen to go to Tel Aviv, perhaps I would have had a different career," Dr. Hasson reflects.

**If you had unlimited amount of money, which disease would you try to develop a stem cell-based cure for?**
"In have studied neural cells and their role in the central nervous system and I think that neurodegenerative diseases have a major need, says Dr. Hasson. "Cardiac cells are also important and the cancer field is interesting as well."

"I have a personal point of view," Dr. Mazooz tells. "I have had a little boy that was born without his thyroid, so that is a clinical area that I would have liked to focus on. He can live a normal life and just needs to take a pill every morning, but naturally that is still an area that is close to my heart." Other than that, ALS and other neurodegenerative diseases that have no cure are important goals. We are living in an aging world and the therapeutic challenges are big," Dr. Mazooz concludes. •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