

# AION Labs Challenge 5: AI Powered Discovery to Enable Molecular Glue Therapies Frequently Asked Questions

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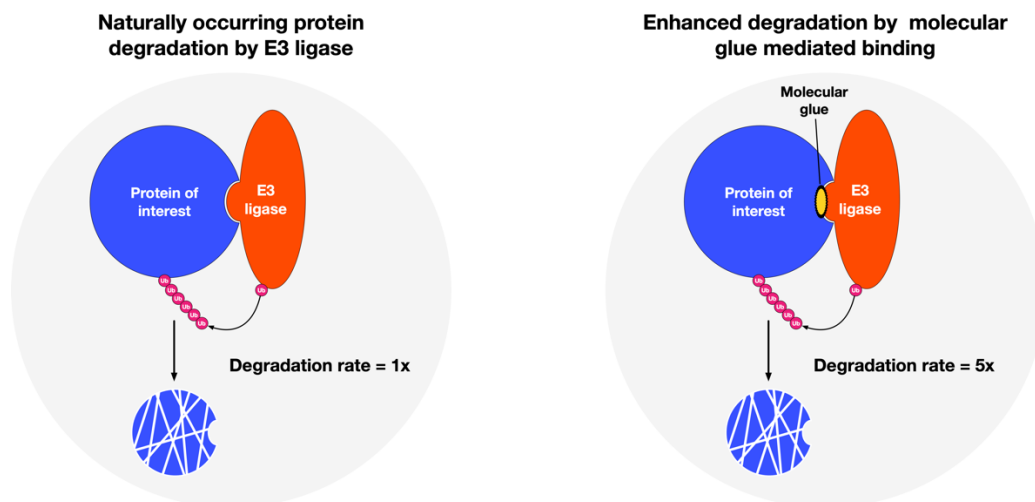
This document compiles many frequently asked questions regarding the specific challenge and the application process. Please feel free to ask any questions we missed at [info@aionlabs.com](mailto:info@aionlabs.com).

## What is this challenge all about?

Proteolysis-targeting small molecules hijack the cellular protein degradation machinery to selectively reduce a target protein's abundance. This new drug modality has the potential to degrade proteins that have been considered undruggable with existing approaches. The field is divided into two main types of molecules: PROTACs (PROteolysis Targeting Chimeras), which are molecules designed to bind a protein of interest (POI) to a chosen E3 ubiquitin ligase (E3); and molecular glues, which are small molecules designed to enhance a natural POI-E3 interaction. Molecular glues are easier to develop as oral drugs since they resemble small molecules that have been developed by pharma for many years.

There are over 600 human E3 proteins that differ in functionality across different tissues, cell types and conditions. This family of proteins control cellular processes by binding other proteins and tagging them for degradation. Once a specific POI is identified as naturally being tagged by an E3, we can design a small molecule drug to strengthen this interaction, thereby increasing the rate of degradation of the POI and modulating disease-causing activities. However, the main challenge for developing such molecules, named molecular glues, is the identification of naturally occurring POI-E3 interacting pairs.

The following figure illustrates how molecular glues are expected to work. On the left, a naturally occurring process within a cell and on the right, enhanced degradation rate enabled by a molecular glue that strengthens the association to E3 ligase.



## AION Labs Boot Camp FAQ

We invite you to propose the development of a platform that enables molecular glue discoveries focusing on the following key challenges:

- An approach to identification of naturally occurring POI-E3 pairs in specific organs, cell types and conditions.
- For a given POI, identify and rank the E3 most likely to degrade it in the specified organ, cell type and condition.
- For a chosen E3, predict the proteins degraded in a specific organ, cell type and condition.
- For a selected pair of POI-E3, provide a 3D structure of the complex to enable the computational design of molecular glue.

### How will you measure success?

The new technology developed by the company will be tested using the protein MYC as POI. There are multiple validated E3 for MYC in the scientific literature and the technology will be employed to test the predicted efficacy of specific E3 to degrade MYC in a variety of cell lines. We also expect to test a few novel E3 predicted to degrade MYC if such will be identified.

### Can you provide an example that will demonstrate the impact of this technology and the complexity to address?

Small molecule drugs were successfully used to inhibit the function of enzymes by fitting into the functional pocket of the proteins. However, many proteins do not have a functional pocket in which a small molecule can bind with high affinity. MYC, used as an example above is such a protein. An additional example include KRAS. The ability to use a small molecule to degrade MYC or KRAS through an E3 will allow us to effectively target such proteins which are hallmarks of cancer. [Here](#) is one example that illustrates the challenges in targeting MYC with existing approaches.

There are several complexities within this challenge. First, showing the a protein can be tagged by E3 is not sufficient. The E3 activities vary across cell types, organs and conditions. In addition, one E3 can degrade many other proteins leading to potential side effects of drugs that employ a specific E3. Secondly, we do not have extensive data where E3 tagging of specific proteins have been documented. Data exists but it is limited and mostly public. Pharma companies do not have extensive data on this type of interaction. Finally, there are no clear and clear cut experimental validation systems that can be easily used. Often, validation is done by knocking out a specific E3 and measuring protein abundance changes within cell lines. This is an indirect type of measurement.

### I have my own great idea. What is the advantage of joining AION Labs vs trying to create my own company?

AION Labs was created to build successful pharma AI companies. Our field is complex, spans many disciplines and validation, which happens in patients, is slow and expensive. To be a successful pharma AI company, we believe that all stakeholders should work together from day one. By joining

AION Labs you ensure that you are working on an important problem for the field with your potential customers. You will have mentors from each pharma company who are experts in the field to guide you, challenge you and test your results. You will also have AWS as a partner to help you design your platform architecture and our VC partner to guide you on the business side and ensure your success as a commercial company. In our model you will be able to focus on the science and prove the value of the platform before you are forced to deal with the business aspect of a company. Once you graduate from AION Labs, you will have a network of partners and customers who know and trust your product.

### **How is AION Labs different from any other incubator / accelerator?**

AION Labs is very different. We are an innovation lab and not an incubator, which means we co-create companies with our candidates. We focus on AI companies in the drug discovery and development space and our team has expertise in that field. We provide substantial funding to get started (\$2M for 4 years), access to vast private data and to experts and mentors in multiple pharma companies. The pharma mentors came up with this problem to solve, they will review the applications and be part of the process to select the founders. They will also be your potential customers and this type of relationship ensures a commitment to your success and a product market fit. In addition, AWS will support you on the technology side and our VC will mentor you on the business side and help you with building your business model. Having all partners work together by your side from day 1, is what makes our model different – we remove the roadblocks and set you up for success!

### **How is equity distributed between AION Labs and my startup?**

The partners who are sponsoring your specific startup (minimum 2) will have direct equity in your startup. AION Labs doesn't have any equity in your company. There are no additional special rights or IP to any of the partners who joined besides equity. The exact equity will be determined based on what you bring with you as you join AION Labs. Our model is flexible, and we promise to be fair. We do not provide specific numbers because it is difficult to setup a one size fits all model. In one scenario, a young and brilliant team can join with just an idea and another scenario is a small company with a technology and even a seed investment. We will negotiate the terms and we promise that our offer will be fair.

### **How do I apply for the challenge?**

Please apply through the BioMed X platform [here](#). The application requires a proposal for solving the challenge. Even if you don't have one yet, **please register** in the system so we can communicate with you while the challenge is open.

### **I am not sure I can come up with a great proposal in the time provided, what should I do?**

We don't expect you to solve this complex issue within a few days in a short proposal. We are looking for proposals that show you understand the main issues of this field and demonstrate your creativity.

You will have a chance to refine your proposals in our boot camp. Don't miss your opportunity to shine!

### **I would love to work in the suggested field but it's not really my field of expertise. Should I apply?**

Yes! The key to team success is diversity. Do your best to bring your point of view in the application and go for it.

### **I am not sure which role to apply for, Group Leader / Scientist Founder or Postdoctoral Researchers / Scientist Co-Founders. Can you explain the difference?**

A startup company will initially have one group lead and two researchers. The group lead is responsible for the startup and the person who will be the leader of the new company. The boot camp winner will be a person who applied for the group lead position. Once the winner is announced, he/she can choose up to 2 co-founders from the boot camp or hire later.

If you wish to lead the startup and have experience beyond a PhD, you should apply as a group lead. However, if you recently completed a MSc or PhD, you have better chances to join a startup team if you apply as a scientist / co-founder.

### **Is the boot camp fully paid for by AION Labs?**

Yes! If you are among the selected candidates, we will cover all travel costs and take care of everything for you including flights, hotel and local transportation.

### **Do I have to attend the boot camp physically or can I participate remotely?**

We believe it is extremely important for you to be present in person. It will allow you to meet other people who might be your co-founders in a new startup. You will also have a chance to visit the place where you will live and work for the next 4 years. Therefore, we require all participants to be present physically in Israel, unless there are very unusual circumstances which prevent you from traveling (visa issues, covid restrictions, etc.).

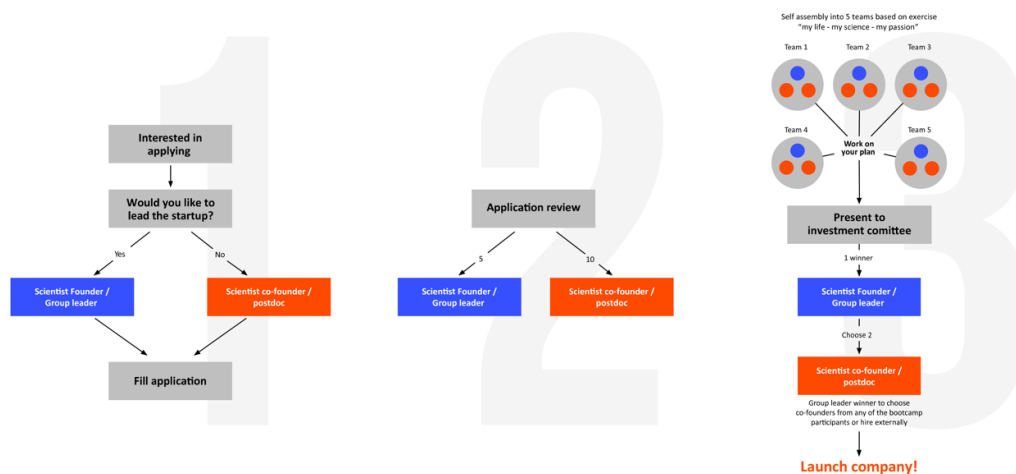
### **How many people are invited to the boot camp?**

We invite 5 group leader / founder candidates and 10 scientists /co-founder candidates.

### **What should I expect in the boot camp?**

The boot camp is all about pushing your proposal to the next stage or starting from scratch and creating a completely new one with your team. We will help you to associate in groups of 3 (group leader + 2 researchers) and you will be working intensively on your proposals with close feedback from our mentors. It is a crash course in how to build a scientific work plan. On the 5<sup>th</sup> day, you will present to our investment committee which will select the winning team and plan.

Below is a schematic of how the boot camp works:



## As a group leader, what happens after I win the boot camp?

Congratulations! As the winner, we will offer you a contract to start your own company in AION Labs. You will be able to choose up to 2 co-founders from the boot camp who will join you (or hire later). In addition, your startup will receive funding in the amount of at least 500,000 USD per year for a period of up to 4 years, free access to our facilities in Rehovot, 100,000 USD cloud credits from AWS, and continuous support from our experienced mentors.

## If I win, do I have to relocate to Israel?

Yes. All our startup teams at AION Labs are required to be present in our innovation lab. The lab is designed in a way that will allow our startup teams to be synergistic when co-localized and this will also be the best way to become part of the Israeli healthcare ecosystem and form strategic partnerships with industry and academia. That said, it doesn't mean that all employees must be local. It will be possible for a startup to hire remotely if needed.

## I heard that Israel is a very expensive place to live. Will my salary allow me to live comfortably?

Yes. At AION Labs the budget allocates industry level salaries to all employees. This is important to allow us to compete for local talent and to make sure you can live comfortably and focus on your work. In addition, it is your company, so you can decide what your salary is.

## Me and my family don't speak Hebrew. Is it easy to communicate with people in English?

Yes. Almost all Israelis everywhere in the country speak English. You will also be part of a multi-national community at AION Labs where everyone will default to speaking English all the time.

## **What about schools and kindergartens? Are there international schools?**

Once you win the boot camp and decide to move to Israel, our team will assist you and your family with everything you need. There are many international schools in Israel since this is a state that has many immigrants every year from many countries. We will be happy to answer specific questions.

## **Can my company grow beyond the initial team?**

Of course! Like any other company, we will support you in raising additional funds and grow. However, at AION Labs we believe in elegant scientific proof of concept before scaling. You have very strong partners who are by your side and can push you a long way – 4 big pharma companies, AWS as your technology partner and IBF as your VC partner. All of us, including the AION Labs CTO, are committed to your success and we will push you forward in solving the key challenges. If the company is successful, we will all be committed to grow it further.

## **I already have a company in this space – Can I join AION Labs regardless of the specific challenge?**

A company cannot apply to our boot camp challenges. Only people can apply as individuals. That said, we have a second track allowing you to join as a company. We only require that at least 2 of our partners agree that your company is solving a key problem in our field. Please contact us at [info@aionlabs.com](mailto:info@aionlabs.com) to schedule a meeting.