

April 25, 2021

To whom it may concern,

I write this reference letter in support of Dr. Razvan Marinescu, currently a postdoctoral researcher at the Massachusetts Institute of Technology (MIT), who is petitioning for permanent residence in the United States based on his extraordinary abilities. Dr. Marinescu is an exceptional scientist and leader who has made contributions of major importance to the field, and I strongly support his application.

I am XX, the XXX at XXX.

I manage a team focused on exploratory data analysis and development of prediction models that improve clinical trials. Before moving to XXX, I was the XXX at XXX, working on assay development projects and discovery of novel biomarkers, which are disease markers used for diagnosis, prognosis and treatment response predictions. I have more than 10 years of experience in XXX in the biopharmaceutical sector. I hold a Diploma in XXXX from the University of XXX and a doctorate from the University of XX in XXX, and have authored more than 20 scientific articles on novel disease markers and statistical methods for predicting Alzheimer's disease and other diseases.

I first heard of Dr. Marinescu's work in 2017, when our team at XXXX decided to participate in the TADPOLE Challenge, which he organized during his PhD at University College London. As part of the challenge, we had to create an algorithm that could automatically predict which subjects, out of a total of 800, would develop Alzheimer's disease in the future. This task was well aligned with our objectives of building computational AI models for early diagnosis of diseases such as Alzheimer's disease. While at XXXXX we had many years of experience with such algorithms, it was not an easy task due to the complexity of the problem. Eventually, we managed to create a good algorithm for making accurate predictions, [XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX]. The impact of the TADPOLE competition in Alzheimer's disease prediction research cannot be overstated: around 30-40 international teams participated in the competition from both academia and the biotech industry, it was backed by the three main Alzheimer's disease charities worldwide (Alzheimer's Association, The Alzheimer's Society and Alzheimer's Research UK), and it entirely reshaped the research field regarding what are the best AI methods for predicting such a disease. In addition, the ability to predict Alzheimer's disease is crucial for our clinical trials at XXXXXXXXXX, because we can more accurately screen subjects to undergo such clinical trials, increase the precision of treatment effect estimates by adjusting for explained variability (predicted by the models), and monitor the progression of subjects in our existing trials.

Dr. Marinescu has been an outstanding leader during the organization and running of TADPOLE. He helped all the teams, including ourselves, understand the problem statement, how to use the dataset, and offered us algorithms to get started with. When we had clarifications, we always reached out to him via email or on the forum. He also analyzed and evaluated all our submissions and worked with us to summarize all our technical methods in the final manuscript. He presented the final analysis at the two main conferences in the field, the Medical Image Computing and Computer Assisted Interventions (MICCAI 2019), as well as the Alzheimer's Association International Conference (AAIC 2020), and the results were received with great enthusiasm by the whole research community.

Dr. Marinescu has also published DIVE[1] (“Data-driven Inference of Vertexwise Evolution”), a well-known predictive model of Alzheimer's disease that identifies highly detailed patterns of pathology in the brain. The DIVE model can be used not only to predict the future evolution of Alzheimer's disease subjects, but also to identify new Alzheimer's disease biomarkers that can be used to diagnose the disease and monitor its progression. My team at XXXXX has been working for several years on developing novel biomarkers of Alzheimer's disease, and I can confirm that Dr. Marinescu's work is of fundamental importance for the research field, and had a significant impact on future development of AI prediction models for Alzheimer's disease. It was, for instance, cited more than 24

times, while the precursor[2] to DIVE, also by Dr. Marinescu, was cited more than 14 times so far.

Dr. Marinescu is also very well-known for his work on disease progression models, a specific class of medical AI models which predict not just the diagnosis of a particular patient, but their entire future progression. He worked on several major research projects in this line of research, such as a major study of Multiple Sclerosis, which gathered more than 106 citations so far, and the SuStaIn model, which characterized the disease variability in both Alzheimer's disease and Frontotemporal Dementia, and which gathered more than 85 citations so far. Given the huge burden of such diseases, currently affecting more than 3 million people in the United States alone, and the lack of suitable treatments, the work of Dr. Marinescu is of paramount importance for healthcare in the US and worldwide and can have even more impact in the future due to increasing prevalence of these diseases.

Given his major contributions in the field of medical Artificial Intelligence, in particular through his scientific publications, Dr. Marinescu is truly among the very top of his research field. His work has had significant impact not just in academia, but also in the biopharmaceutical industry, best exemplified by the fact that our company XXXXXXX put together a team to participate in his challenge and build an AI prediction model for Alzheimer's disease. Moreover, his research work has impacted not just Alzheimer's disease, but many other diseases such as Multiple Sclerosis and Frontotemporal dementia, which are major healthcare challenges of our times and into the future.

To conclude, Dr. Marinescu is an outstanding scientist of extraordinary ability in the field of Artificial Intelligence in Medicine. I strongly support his efforts to petition for permanent residency in the United States, and I can guarantee that he will be a valuable asset for the country.

Yours sincerely,

[1] Marinescu, Razvan V., et al. "DIVE: A spatiotemporal progression model of brain pathology in neurodegenerative disorders." *NeuroImage* 192 (2019): 166-177.

[2] Marinescu, Razvan V, et al. "A vertex clustering model for disease progression: application to cortical thickness images." *International conference on Information Processing in Medical Imaging*. Springer, Cham, 2017.