Applying Engineering Discipline to Mechanistic Mathematical Modeling and Analysis Services, Applied BioMath, LLC. is enabling Biotechnology and Pharmaceutical Companies to De-Risk Projects and Accelerate Development of best-in-class Drugs into the Clinic

John M. Burke, PhD
Co-Founder, President and Chief Executive Officer
Applied BioMath, LLC.
www.AppliedBioMath.com

Contact:
John M. Burke, PhD
617-914-8800
john.burke@appliedbiomath.com

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

CEOCFO: *Dr. Burke, would you tell us the focus right now at Applied BioMath?*
Dr. Burke: Our focus continues to be brand recognition, market visibility, growing our team, and being the best at what we do. We see evidence of our market penetration growing which is great. For example, customers are coming to us now outside of our personal network and saying they have to work with us because we are the best in the world at what we do. It has been a concerted effort to earn the trust of our peers and we do not take that for granted.

CEOCFO: *What has changed over the last year that people are recognizing the value? Is it the industry itself or just the volume of engagements? Does it even matter as long as it is happening?*
Dr. Burke: That is a good question. I think the primary factor is that word is spreading that we are doing an excellent job. We have been in the news frequently over the last year announcing collaborations and awards. Each new team we work with helps spread the word about the return on investment of our work. In most instances we save our collaborators a lot of money in a short period of time. For example, we save six months to a year in R&D and maybe $500 thousand to $2 million. That is a big deal for an early project in research. Other times we accelerate a clinical trial design by up to three months by justifying a higher starting dose which is a big deal for small companies and patients as well as investors. Word is spreading that we are doing trusted, valuable science.

Secondly, I do think that the industry is a little more receptive to these approaches right now. The FDA has even stated they want more mechanistic approaches. One of our goals all along is to create a new engineering discipline in biotechnology and pharmaceutical science, such as what you would see in electrical engineering, chemical engineering, computer science, and mechanical engineering. Engineering approaches de-risk projects, save money, and accelerate the evolution of these fields. There are just way too many failures in our field and it is too expensive. We need these engineering approaches to help decrease the failure rate from 95 percent to 85 percent, save six months to a year in R&D, and decrease the rate of late-stage attrition.

CEOCFO: *What is the key to putting together the various components of how you work?*
Dr. Burke: We are very collaborative with our partners and within Applied BioMath. We have a strong core of diverse scientists across many disciplines. Our project teams typically have at least one to two mathematical modelers as well as at least one biologist. If the project requires us to create and modify our internal software, we have software engineers to do that. While everyone is an expert in their specialty, our team members have diverse experience and understand each other's disciplines. For example, our biologists are experts in biology but also are adept at understanding and communicating about modeling and software. Likewise, for our other specialty areas. This helps us work seamlessly as a

team while covering the broad bases of biology, pharmacology, software, and mathematical modeling involved in most projects. Also, every team member we hire is innately collaborative, or they wouldn't fit well on or team. We work diligently to have standard operating procedures that focus on best practices for collaborating and communicating. All of these pieces factor into using putting together the components of our work.

CEOCFO: *How do you stay up to date on what is happening so you have all the latest science to put into the model?*
Dr. Burke: We are all scientists. We are 80% to 90% PhDs in this company. Anyone who goes into this field likes to read and learn about new science. It is what leads us to this field. As a company, we encourage our team members to read new literature, to publish papers, and to write grants internally in line with our strategy. We also encourage our scientists to go to scientific conferences. This is all important; by continuous improvement, and continuous gathering of knowledge. We have weekly internal meetings where we share science and internal modeling classes and scientific seminars to keep everyone up to speed with what is going on in the field. We work with partners to read as many papers as we can and get a guided scientific tour so we can have accelerated learning on their therapeutics and indications. We try to be fast, efficient and topnotch.

> **"This approach can be applied to any project, from assessing risk, developing a drug, trying to predict optimum drug parameters, accelerating the development of Best in Class drugs, lead generation, prioritizing experiments and helping with experiment design, helping with clinical candidate selection, helping with GLP tox design, helping with the IND, Phase 1, II and III prediction."- John M. Burke, PhD**

CEOCFO: *Many people who talk about AI claim there is no way to get all the information without it, particularly in medicine and science, and that you absolutely have to have AI to get everything. Why is it better to for people to find and review info?*
Dr. Burke: We really do not do much artificial intelligence; we do mechanistic modeling of the drug, mechanistic modeling of how they mechanistically work together. This is like building a weather model but instead of modeling the aerodynamics and the fluid dynamics in clouds and patterns, we are modeling how cells interact with drugs, cells with cells, and receptors, and ligands, etc… Our approach is more akin to modeling the shooting of a rocket to the moon or predicting weather patterns than it is in straight up AI. Sometimes AI helps support our projects, and maybe streamline some data from what is the most important data. However, the benefit of what we have is we take things like time and dynamics and we can leverage biology mechanisms. This is a dynamic contextual process. We are not just a straight-up AI company.

CEOCFO: *Applied BioMath offers a personal approach as your people are so knowledgeable, along with the model that you use. Does that approach make a big difference?*
Dr. Burke: Yes, I think this is one reason why we have such a high repeat business rate, which is over 80% repeat business. We constantly get feedback that we are very professional, kind, thoughtful, and that we can take scientific criticism well. We deliver scientific criticism well. I think we can do that because our leaders have worked in pharma and biotech for decades. As a company, we have over 100 cumulative years of industry experience. When we hire and train our fresh PhDs, an important component is whether this person is kind and personable; not just knowledgeable. It goes back to some critical advice that my Post Doctoral mentor and advisor at MIT gave me, Douglas Lauffenburger, PhD. I asked him why he was so successful and one of the pieces of advice he shared, amongst many, is that he does not necessarily hire the smartest people, he hires the nicest people. That has always stuck with me.

CEOCFO: *Are there particular types of projects that you prefer?*
Dr. Burke: Our modeling approach can be applied to projects across the entire customer workflow from early research to clinical. Our projects look at what mechanisms of the disease and drug are known, what questions the project team are trying to answer, what data they have, and their timelines and we then come up with the best mathematical strategy for the project. This approach can be applied to any project, from assessing risk, developing a drug, trying to predict optimum drug parameters, accelerating the development of Best in Class drugs, lead generation, prioritizing experiments and helping with experiment design, helping with clinical candidate selection, helping with GLP tox design, helping with the IND, Phase 1, II and III prediction. The list is long! When you have that single model that has started to recapitulate all your preclinical data and competitor data or comparator data, it is a powerful mechanism and you want to help more and more to make better decisions more quickly.

CEOCFO: *How do you know when it is time to give up?*
Dr. Burke: I think we are lucky in our field that in a lot of ways it is still early, meaning many scientists and executives use their gut for experience to do these computational non-linear approaches in their brain and it is difficult. I think as long as

we are better and faster than the back of an envelope calculation, we are always going to be providing value and de-risking. I think this is exactly why we have been so successful and receive such positive feedback from our customers. When we work with our partners to vet their questions, we look at their questions and timelines, examples of their data and competitor's data, how they think the biology works in the context of the drug, how they think the drug works, etc. We look at that and if we do not think we can help for some reason, we just do not work on the project, we weed it out. We want to make sure that if a customer is going to invest in us, we can deliver for them.

CEOCFO: *I see from your website that giving back to society is important to you. How do you decide where to focus your efforts?*
Dr. Burke: We knew from the get-go that supporting our community was important to us so we put a statement in our operating agreement that we give a certain percent to charity annually. We take suggestions from all of our employees on which charities to support and the founders sit down and look at the list and finalize the charitable giving. We try to support all team members' suggestions as long as nothing is too controversial and as long as it is for the betterment of society.

CEOCFO: *What is next for Applied BioMath*
Dr. Burke: More market penetration and brand recognition. We have to grow and grow carefully and smartly. We are in the middle of our fifth year and we are looking at our next two years for our goals and are we fulfilling those roles. We are staying the course and constantly trying to learn.