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Applied BioMath is Focused on Growing its Team of Industry Leaders to better Meet the Needs of their Biotech and Pharma Customers using Mathematical Modeling to De-Risk and Accelerate Drug Development

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CEOCFO: ***Dr. Burke, last year when we spoke, you indicated you were working on brand recognition and growth. How has that worked out? What are some of the highlights this past year for Applied BioMath?***
Dr. Burke: Applied BioMath needed to focus on growing our team to meet the needs of our clients. I am happy to say we are presently at 32 employees and we are on track to be close to 40 by the end of this year! We are committed to growing our team responsibly so that our growth is sustainable and our deliverables remain high quality. We always consider our business model and we never hire ahead of our business model.

Our growth plays a role in our brand recognition. Several of our most recent hires, including Alison Betts and Helen Moore, from Pfizer and AstraZeneca, respectively, are leaders in our industry. The fact that they came to work for us says a lot about their belief in our brand and value. We've also increased our brand awareness through advertising on local NPR stations, presenting at scientific conferences, and hosting our own events. We host a free scientific meeting in our field that is highly regarded, and this year we had well over 100 attendees at our meeting. So, it's safe to say our brand recognition is coming along quite nicely.

CEOCFO: ***Would you tell us about Applied BioMath?***
Dr. Burke: Applied BioMath uses systems pharmacology and mechanistic modeling to help pharmaceutical and biotechnology companies better understand their therapies and targets and how their therapies interact with the targets and disease. This helps teams decide what therapeutics are likely to be the winners, so they do not waste time and resources pursuing those probable failures. Once winners are selected, it becomes about how we can make the therapeutics better and get them to the clinic earlier, with the right dataset. Therefore, our clients are more likely to have a best-in-class drug, and hopefully a first-in-class drug, but also they will more likely have a successful clinical trial.

CEOCFO: ***Who is turning to you, when might they come and what do you provide?***
Dr. Burke: The majority of our new partners, who we have never worked with before, come to us for support for their investigational new drug (IND) filing. They have very complex drugs, where traditional approaches cannot work for their drug's complex mechanism of action, so they have to do simulations to support their starting dose and maybe their dose escalation, which are critical parts of an IND. That is typically why they come to us first. Once they work with us and see how we can scan through multiple parameters in a very high dimensional space, they see the value proposition of coming to us earlier in the pipeline. For example, we can look at the number of cells, sites per cells, reaction rates and drug affinities, and potential patient variability. This includes the most cutting-edge therapies, including cell therapies like CAR T cells, multi-specific antibody drug conjugates, CRISPR/CAS9, T cell engagers, engineered mRNA, and conditionally active biologics.

Typically for the second and onward engagements, we might then come in much earlier to help look at a new drug proposal and help answer questions such as:

- What are the pros and cons of hitting certain proteins or targets in the disease pathway?
- Which target is potentially the easiest to drug and which are the most difficult?
- What are the most sensitive model parameters which impact your next steps in prioritizing experiments and experiment design?

It can also enable lead generation. It is very systematic because we can account for mechanism. There is really no other way to do that. This enables our partners to accelerate into clinical candidate selection, then IND, and eventually into the clinic.

CEOCFO: ***When a company engages with you, do they typically pay attention to your results?***
Dr. Burke: Absolutely! We know they listen to our results because we see our clients do the experiments to try to support or refute the model predictions that we make, which is what we want. Our work is part of the scientific process and thus has to be engaged properly with experiment design. This engagement and belief in our results is further evident in our higher than 80% repeat business rate. If the groups did not use our results or listen to them, they would not come back for more.

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CEOCFO: ***Is it a little easier for you to attract talent as Applied BioMath is innovative in your approach or is it as difficult as it is for everyone else?***
Dr. Burke: It is difficult to attract talent as we are competing with the largest pharmaceutical companies, but we are attracting the talent anyway. My friends at large pharmaceutical companies give us a friendly "hard time" because we are stealing many of their hires. I do think we attract talent because we are innovative, but also in my opinion, if you are a modeler within a large pharma, you are still a service provider within that large pharma. It is hard to be rewarded for your innovation as a mathematical modeler in that situation. When you work for a mathematical modeling and simulation company, where we do this day-in and day-out for over 40 companies, on over 100 projects in the past five years, we can award our employees for being innovative in our space. I think that is very important.

CEOCFO: ***Would you give us an example of what innovation means for you; what you have learned over the past year that has made a difference in your overall approach?***
Dr. Burke: Everything that we are doing is innovative. For example, last year our revenue was roughly 50% from large pharmaceutical companies and the other 50% from medium sized biotechnology companies or smaller. For the smaller companies, by definition because they are VC backed, they need to have exciting IP. That often relates to very complex mechanism of action and innovative throughout their therapies. Whether they are T-Cell engagers, multi-specific ADCs, or other complex cell therapies, it is hard to understand the combinatorial effects of all the different drug properties in the disease. It is very difficult to wrap your brain around this without modeling and simulation, and in particular, mechanistically modeling how the drug works in patients.

Every time we work on a project it is innovative because the biology and drugs are so cutting-edge. We accurately represent the biophysics of the disease and the drug on the timescale and with data that you could possibly generate, which helps inform valuable decisions. Every time we do that it is new and innovative, because there is so much cutting-edge research out there, which we remain on the forefront of.

CEOCFO: ***How do you show the results?–What are you presenting to your client? Are you able to help them put the info into terms to attract investors and get health community interested?***
Dr. Burke: Certainly. We receive feedback from our early partners that when they approach VCs for funding, the VCs strongly encourage the company to work with us because we will increase their likelihood of success. We have helped the

VC's asset companies for the past five years and the VCs are seeing the results. That is part of our brand awareness and a part of our being good partners. For our partners who already work with us and approach VCs, they receive positive feedback for working with us and in some cases receive a better valuation.

As for what and how we show results, when we work with our partners and build the mathematical model, it's a collaboration. Together we go through the literature and collaborate to make a picture or a model diagram of what we are going to mathematically model. Already we present value because we are helping our partners better understand the mechanism of their disease in the context of their therapeutic concept. We then codify the model diagram into biochemical equations which we then translate into systems of mathematical equations. Therefore, we are helping them understand the complexity of their disease and in building this together they understand it and start to trust the model. We also help them better understand data because the data can be very complex. Throughout this process, the mathematical model can act as a central repository of data and hypothesis to help tell their story and understand this complex data in the hopes that you will have a better IND and/or a better transition if and when the biotechs partner with large pharma.

CEOCFO: ***Is there competition? Are people trying to replicate your approach?***
Dr. Burke: There certainly are other companies out there. They tend to focus solely on very, very large models, which is not our singular focus. Our biggest competition will be in large pharmaceutical companies that have similar groups that do what we do, but they continue to bring us in to help as extra resources.

CEOCFO: ***What is it about your model that is different/better than what might be available at big pharma?***
Dr. Burke: One advantage that we have is that we have been very fortunate with the help of Federal Grants, SBIR, NIH Grants, which have enabled us to develop our internal technologies that help increase our capability and capacity. For example, with some of this funding we have developed an Alzheimer's Disease drug model where we are co-drugging a small molecule, prescribed daily, and a large molecule, dosed every week or every two weeks. We simulate these scenarios for over 40 or 50 years, for over 50 simulated patients. Using existing technologies, that might take 2, 4, 6 or 8 hours depending on the complexity. With technologies we've developed, it can execute in 2 to 3 minutes. That is a big difference! If I have to wait 2 to 6 or 8 hours to run a simulation, I am a bit more hesitant to explore multiple scenarios. What happens if this protein goes up? Or this synthesis rate changes? Or this ligand expression goes down? Or the cell numbers change? If I only have to wait 3 minutes, I can consider as many scenarios as needed and then do some of these numerical thought experiments much more quickly. That has helped us out quite a bit.

Another thing that has helped us is that we are working with so many different companies, large and small, from very early to very late stage, where sometimes they are far out as into Phase 3, and we are seeing how so many different companies think about the R&D process. That enables us to be better scientists. Each company approaches drug discovery and development differently. If we can see how 40 different companies on over 100 projects can work to get into the clinic and what they are doing in the clinic, that gives us a broad spectrum of different ideas, which makes our analysis better.

CEOCFO: ***What do you show people at conferences? How do you get people to your exhibit?***
Dr. Burke: Most of the work we show is based on approved case studies that highlight collaborations with our partners, so we have to get permission. These are real scientific projects with novel results, sometimes counterintuitive results. The science is what attracts scientists. We can also show work that we have done on our own funding, and/or work that we have done based on work that we have gotten from Federal Grants.

CEOCFO: ***Put it together for our readers. Why pay attention to Applied BioMath?***
Dr. Burke: We are developing a new engineering. This is in line with people like Douglas Lauffenburger, PhD, at MIT, and Peter Sorger, PhD, at Harvard Medical School, and a few others, where we are developing a new engineering that is applied to drug discovery and development. This is no different than aeronautical engineering which helped make better airplanes, or electric and computer engineers which helped make better computers, or mechanical engineers which helped make better cars. We need mathematical models to make better predictions, to accelerate the scientific process, to make things better, and I think we are doing that now as a new engineering field.

It is exciting to be at the forefront of a new discipline. As we continue to move forward, everyone will be doing this in the next few years. This will become part of the standard process of making drugs better and eventually will help reduce late stage attrition rates, hopefully saving hundreds of millions of dollars. With any luck, we will help our industry still do the best research in the world, still have well paid scientists, and at the same time reduce drug costs.