Interview with Mark Tracy: Insights into the Biopharmaceutical Industry

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Mark Tracy served as president of the Controlled Release Society (CRS) from 2010 to 2011 and on its Board of Directors (BOD) from 2008 to 2012. He also served on the CRS Board of Scientific Advisors from 2002 to 2005 and was a cochair for the CRS Annual Meeting in New York City in 2008. Highlights of his term as president and member of the BOD include establishing of the CRS College of Fellows, updating CRS governance and the strategic plan, and the launch of a new journal (*Drug Delivery and Translational Research*), a new book series, and a new website. He also helped open a new CRS chapter in China and, as president, hosted the 2011 CRS Annual Meeting comprising approximately 1,400 delegates.

Dr. Tracy is a fellow of the American Institute for Medical and Biomedical Engineering (AIMBE).

Dr. Tracy has made significant contributions in the field of biopharmaceuticals. Dr. Tracy played a key role in the advancement of nine programs into the clinic, including several that were commercialized: Nutropin® Depot, Risperdal® Consta, Vivitrol®, and Bydureon®. He is well known for successfully bringing new protein, peptide, nucleic acid, and small molecule based medicines to the clinic, incorporating recent advances in drug delivery, nanotechnology, and targeting. He has played important roles in the development of technology platforms and product pipelines for Alkermes, Inc., and Alnylam, Inc., two leading biotechnology companies, where he worked for over 20 years in various leadership roles of increasing responsibility. At Alkermes, he played a key role in building the company's parenteral product development capabilities and was a member of the team that developed the first sustained delivery system for proteins approved by the FDA. While at Alnylam, Dr. Tracy successfully brought to the clinic new nanotechnology-based products that enabled human clinical proof of concept for RNAi and a growing pipeline of clinical programs.

Before joining the biopharmaceutical industry, Dr. Tracy secured his bachelor of science in chemical engineering *summa cum laude* from the University of Illinois at Urbana-Champaign and received an M.S. in chemical engineering and Ph.D. in chemistry from Stanford University. Dr. Tracy also attended an executive program in business administration and management at MIT Sloan School of Management.

Dr. Tracy is founder and president of Tracy BioConsulting, LLC (www.tracybioconsulting.com), where he provides consulting services to biopharma clients, helping them to plan, build, and navigate a successful path from the research stages through the clinic for new platforms and drug programs, including those involving novel drug delivery systems, nanotechnology, and targeting. Also, Tracy BioConsulting provides access to an extensive network of CROs and CMOs and help in the identification of new business opportunities and creation of value from technology platforms. Tracy BioConsulting clients include startups, small and large biotech and pharmaceutical companies, CMO/CROs, and investment and VC firms.

Q *How did your educational journey lead to a career in the biotech industry?*

A When I was a kid in grade school, I remember declaring, as soon as I could pronounce the word, I wanted to be a paleontologist. Of course, finding a long-lost dinosaur skeleton was cool to me but probably more so was the act of discovery and learning that came along with it. Over the years, with many great teachers in elementary and high school and a dash of practicality added courtesy of my parents ("How many jobs are there in paleontology?"), I became interested in math and science, chemistry and engineering in particular. I was excited

Mark. Tracy receiving the CRS president's gavel from Diane Burgess at the CRS Annual Meeting in Portland in July 2010.

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to see that, when I applied to college at the University of Illinois at Urbana-Champaign, there was actually a major combining both chemistry and engineering. I was accepted, and off I went as a chemical engineering major. I was fortunate that Illinois was then and is today one of the top universities in the world in the chemical sciences and fostered close interactions between chemistry and chemical engineering. Three professors were particularly supportive and influential in my career direction. Prof. Steven Zumdahl strongly supported me and encouraged my interest in chemistry. He provided me with an opportunity to work in his lab over the summer after my freshman year doing research for the first time. Prof. Tony McHugh introduced me to polymer science and encouraged me to consider graduate school. Prof. Charles "Chip" Zukoski sparked my interest in particles and colloids and provided me the opportunity to do a senior thesis with him, which led to my first published paper. Chip's mentorship and the fun of discovery I experienced in his lab inspired me to go to graduate school at Stanford University. My experience at Illinois also taught me that I was particularly interested in research at the interfaces of traditional academic disciplines, for example, nanotechnology (also known as colloid science), polymer chemistry, and engineering. Like Illinois, Stanford also fosters close interaction between chemistry and chemical engineering. I was fortunate to combine my interests in polymers and colloids working in the lab of Prof. Robert Pecora using optical methods to study diffusion in complex fluids. Bob connected me with members of industry with whom I worked on a couple projects complementing my thesis work. Through Bob's mentorship, I honed my research and problem-solving skills as well as developed an interest in collaborative applied research with industry. So as I was about to graduate with my Ph.D., I searched for emerging interdisciplinary fields with interesting industrial applications and opportunities for discovery where I could apply my new knowledge and skills. I read an article on Prof. Robert Langer of MIT, the drug delivery field, and an emerging company he founded called Enzytech, his first startup (now he has founded more than 25). I was fortunate. Enzytech was looking for an entry-level Ph.D. scientist, and I got the job. I moved across the United States from Palo Alto, California, to Cambridge, Massachusetts, just a few weeks after defending my Ph.D. and began my career in the biotech/drug delivery industry.

Q *As a new Ph.D., what was it like to work in biotech startup?*

A Working in a startup is hard work but very exhilarating. Soon after I joined Enzytech, it merged with another startup, Alkermes, Inc. Both were exciting places to work. Things moved very fast. Our mission was to develop sustained release products based on a novel patented encapsulation process. We were blazing new ground in delivery science, including new ways to stabilize proteins, new approaches to control release from degradable polymeric particles, methods of characterization and formulation screening, new processing approaches, and regulatory precedents. It was fun and tough at the same time. There was the sense of discovery that I love combined with a focus on producing products to benefit patients. The sense of ownership and responsibility and the opportunity to make a difference in this environment were very motivating to me. In a way, this phase of my career was my "boot-camp" in pharmaceutical product development, the regulatory approval process, and building a biotech company. I was especially fortunate to work with and learn from great leaders and mentors including Howard Bernstein, Steve Zale, Jim Wright, Robert Breyer, Richard Pops, Prof. Bob Langer, Prof. Alex Klibanov, and many others. Over the period I was at Enzytech/Alkermes, I was a key member of the team that developed the first long-acting protein product approved by the FDA, Nutropin® Depot, as well as several other products that were commercialized: Risperdal® Consta, Vivitrol®, and Bydureon®.

Q *You successfully made the transition from a laboratory scientist role to a management role while at Alkermes. How did this come about? What kinds of challenges did you overcome?*

A There are two key aspects that aligned in my case that enabled my transition from lab to management: first, I came to realize, based on my work experience, that I enjoyed leading science and programs through others as a team as much or more than the direct hands-on work in the lab and, second, my projects advanced and the company grew, creating management opportunities both as group or department heads and project team leaders. I was fortunate to advance from an entry-level Ph.D. scientist to director of formulation development over my time at Alkermes. There were so many challenges: some technical, many related to the business. On the technical side, I recall discovering that our standard *in vitro* release method used for formulation screening was not an adequate predictor of release *in vivo*. This led us to transform our formulation development approach from one based primarily on screening formulations using an *in vitro* test to using a rodent *in vivo* model that was predictive across species from rodents to humans. I also found that the end group chemistry of the polymer is a key formulation parameter impacting release from poly(lactide-co-glycolide)-based particles leading to the development of improved formulations. I played a key role in scaling-up our lab scale process to one that was suitable for making lots aseptically at clinical and commercial scales. On the business side, we were very fortunate to have raised enough funds to progress our R&D work through some very challenging investment periods and regulatory and partnership setbacks. Having a small portfolio of products and technology platforms proved very helpful in overcoming setbacks on individual projects.

Q *Please share some of your lessons learned from your experience in advancing nine biotech products to the clinic and several to commercialization.*

A Here are a few important lessons I learned:

1. Have a detailed plan—at least 2 years for pre-investigational new drug (IND) programs, longer for later

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stage programs—and have a backup (or better yet, several). The path to clinic and commercialization is long, with many potholes along the way. Some are technical, but many are business, regulatory, or clinical in nature. Try to anticipate as well as you can what may trip you up by regularly clarifying and aligning on your program's risks and assumptions with your team.

2. Use a science-based approach in product development. Understand to the best of your ability why each component is in your product, the most important product and process parameters impacting your product's safety, efficacy, and stability, and establish robust assays to characterize your product. These assays are your eyes and ears. Your dividend will be greater credibility with partners and regulatory agencies.
3. Be flexible and adaptable. The technology you begin with as a startup or small company is very often not the technology around which the company is ultimately built. So always be on the lookout for something better, and never close your eyes to the challenges with your technology. Challenges are also opportunities for invention.
4. Celebrate along the way with your team. Recognize the many significant accomplishments on the way to the IND, clinic, or commercialization, not just the big ones at the end.
5. Drug product development is a team sport. No one person develops a drug. High-performing teams do. The career advancement and incentives in your organization and for your team should reflect this fact.

Q *How did you get into the RNAi field? Where is the field headed?*

A I learned of an opportunity at Alnylam, Inc., a leader in the RNAi field, and was very interested to be a part of this new emerging field and company where solving delivery challenges was front and center to enabling new medicines. In RNAi, delivery to the cytoplasm inside of the cell is required. My job was to advance the delivery science and build the capabilities to turn RNAi science into products. I was very fortunate to have the opportunity to build and lead an international team of academic and industrial collaborators that developed new materials and formulations and advanced them successfully to the clinic. We were among the first to demonstrate RNAi in humans and built a pipeline of products with the potential to address serious medical conditions, including rare diseases such as TTR amyloidosis, metabolic diseases such as hypercholesterolemia, and blood diseases. I think the future of the field is bright. Over the next few years, the companies working in this field will advance the first RNAi-based therapeutics to phase II/III clinical trials and commercialization. This progress will stimulate increased interest in the field. However, delivery outside the liver and tumor tissue remains a significant challenge. Over the next few years, I hope (and think) we will see important advances in understanding delivery to different tissues and organs, which will begin to open up new biological targets for RNAi-based medicines. I expect that members of CRS will play key roles in these advances. Stay tuned!

Q *Please tell us about your plan with Tracy BioConsulting, LLC.*

A My passion is developing new medicines and products. Over the years, I have advanced nine medicines to the clinic including four that have been commercialized, including peptides, small molecules, nucleic acids, and proteins. In addition, I have been fortunate to help build two successful companies. I founded Tracy BioConsulting to provide my clients with the knowledge, experience, and connections I have developed from these and other experiences and to help them develop important new medicines. My clients include startups, small and large biotech and pharmaceutical companies, CMOs/CROs, and investment and venture capital firms. Please visit my website to learn more: www.tracybioconsulting.com.

Q *Given your experience with startups and small emerging companies, what advice would you give to entrepreneurs starting up or building a small biotech company today?*

A Prof. Bob Langer, who has started over 25 companies since Enzytech, has boiled down his formula for startup success to the following key ingredients:

- a breakthrough idea published in a top journal such as *Science* or *Nature*,
- a patent, ideally blocking,
- *in vivo* proof of principle,
- capability to have more than one product, that is, a platform, and
- passion.

Enzytech/Alkermes and Alnylam had all of these components as startups! In addition, I would add the following:

- Talk to as many people as possible who have built companies before and learn about their experiences. There are so many routes to success, so ultimately you will have to determine the path that is best for you and your company. For many of us who have science and technical backgrounds, it is also a great way to gain an understanding of the practical business aspects that you will need to build your business and raise funding.
- Know your market, key customers, and potential acquirers, not just your technology. For delivery scientists in biotech, that means you must engage biologists, clinicians, and potential customers and acquirers to understand biological targets, unmet clinical needs, and the value of your product or technology to those customers and acquirers.
- Avail yourself of the many excellent resources that exist today to support entrepreneurs and small company leaders, including the Kauffman Foundation (www.kauffman.org) and local groups in your community such as the Capital Network (www.thecapitalnetwork.org) in Boston.

Q *What accomplishments are you most proud of during your time on the CRS Board and as CRS President?*

A CRS has always been my "home" professional society. It was an honor to serve on the CRS Board from 2008 to 2012 and as CRS president for 2010–2011. I am particularly proud of working with my colleagues on the Board to establish the College of Fellows to recognize leaders in our field and our society, to launch a new website to enhance the ability of CRS to meet the needs of our members 24/7 worldwide, to launch new publications including a book series and the journal *Drug Delivery and Translational Research*, to install new chapters including one in China, and to update our governance and strategic plan to strengthen the society for the future. These efforts are already helping to enhance the society's ability to bring delivery science and technology to its members throughout the world. I look forward to seeing the society continue to develop and grow in the coming years.

Mark Tracy receiving the Distinguished Service Award at the 2013 CRS Annual Meeting. Left to right: Ian Tucker, Mark Tracy, and Kazunori Kataoka.

Q *What do you enjoy doing when you are not doing biotech?*

A I particularly enjoy the arts, travel, and the outdoors. I sing in a chorus. We sing all kinds of classical music and perform throughout the Boston area several times a year. Right now, I am quite excited because my chorus was recently selected to perform with the Boston Pops next December, which is a great honor. I enjoy all forms of travel from taking short drives near home in the Boston area to visiting destinations all over the world. I have really enjoyed attending the CRS meetings over the years because, in addition to the great science and networking, they are always in amazing places to visit. Hawaii is an excellent example! I also love the outdoors and go on hikes whenever I can. Thank you so much for inviting me for this interview. I enjoyed it very much! ■

More Educational Opportunities from CRS

These CRS workshops will take place at the 2013 AAPS Annual Meeting & Exposition
November 10–14, 2013
San Antonio, Texas, U.S.A.

Introduction to Microencapsulation Technologies Workshop

Knowledge of multiple encapsulation technologies and how they are applied is valuable information for developing new products or solving existing problems. It is important, at a minimum, to have a basic understanding of all commonly available processes and their applications. This workshop provides an introduction to common micro- and nanoencapsulation processes and their various applications. The workshop is structured to 1) introduce common encapsulation techniques, 2) review common materials, and 3) provide an overview of the wide range of applications for controlled release products.

Workshop Organizers
James Oxley, Southwest Research Institute, U.S.A.
Irwin Jacobs, Particle Dynamics International, LLC, U.S.A.

Mitigating Risks for Patients When Developing Oral Controlled Release Dosage Forms Workshop

The focus will be to understand the possible risks to patients and approaches to manage them when developing oral extended-release (ER) dosage forms. The discussion will relate to the design, development and manufacture of commonly used ER systems. Industry leaders and subject matter experts will provide scientific basis to the material science, formulation, and process attributes that will help to mitigate risks, under the umbrella of quality by design (QbD). The overall goals of such approaches are to improve quality, reduce costs, but maintain patient safety and treatment.

Workshop Organizers
Ali Rajabi-Siahboomi, Colorcon, U.S.A.
Mansoor Khan, CDER, USFDA, U.S.A.

Register online at www.aaps.org. Information about these workshops is also available on the CRS website at **controlledreleasesociety.org**.