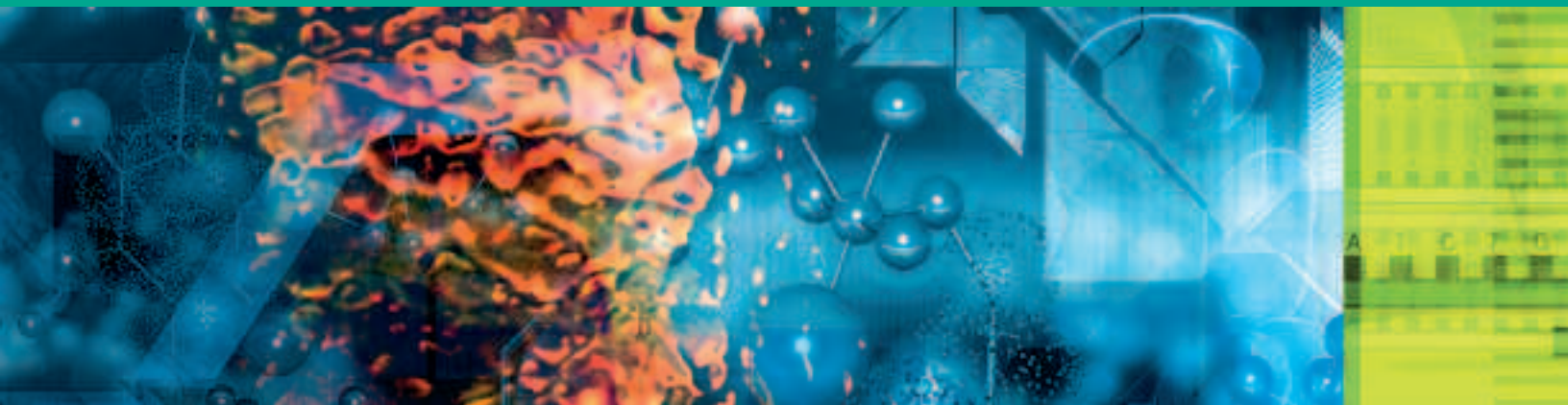


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2007 Compensation and Entrepreneurship Report in Life Sciences

2007
((ABRIDGED VERSION))







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We are pleased to present the 2007 edition of our Compensation and Entrepreneurship Report in Life Sciences. This Report includes summaries and analysis of compensation data collected from 166 private companies from across the country in a wide variety of industry segments: Pharmaceuticals, Therapeutics, Diagnostics, Devices, Bioinformatics, Genomics and Molecular Technologies. The survey data was collected between June and September of 2007.

Our inspiration for creating this survey was a direct response to our clients' requests for better access to reliable, comparable compensation data to assist them in the critical decisions involved in attracting, motivating and retaining key executives at private companies. Over the years we have been able to present the correlation between executive compensation and a number of variables, including financing stage, company size both in terms of product stage and headcount, founder/non-founder status, industry segment, and geography. We have also been able to provide a number of analytics on how an organization evolves with additional financing, Boards of Directors compensation and make-up, and a granular view at company equity plans.

This study was produced by professionals at WilmerHale, Ernst & Young and J. Robert Scott. We were assisted in our work by academics from the Harvard Business School. Our survey has evolved over the years based on input received directly from the industry, and our hope is to continuously improve our data so that we can best serve the needs of our clients in the Life Sciences and Medical Device industries. In that regard, we encourage readers of this publication to submit comments and suggestions to help us most efficiently and accurately present the compensation dynamics of the market. Suggestions and comments should be directed to Mike DiPierro of J. Robert Scott, mike.dipierro@fmr.com.

Participants have been provided detailed data results at no charge. You may secure a copy of the detailed report for \$500 plus a commitment to participate in our next survey. Contact Mike DiPierro of J. Robert Scott at 617-563-2770 or mike.dipierro@fmr.com to obtain the unabridged results. You may also access these summary level results from our website at www.compstudy.com for no fee. We appreciate your professional courtesy in providing proper attribution when citing study results.





Welcome to the 2007 edition of our annual Compensation and Entrepreneurship Report in Life Sciences. This Report – our fifth annual in Life Sciences, and our largest to date - includes summaries and analysis of compensation data collected from more than 1,000 executives at over 165 private companies from across the country in the pharmaceuticals, therapeutics, bioinformatics, genomics and molecular technologies and medical devices/diagnostics segments. Also inside are engaging interviews with two leaders in the Life Sciences industry: Stanley Lapidus, serial Founder and currently Chief Executive Officer of Helicos BioSciences, and Dr. R. Sanders “Sandy” Williams of the Duke University School of Medicine.

This survey was conceived as a direct response to our collective clients’ requests for better access to reliable, comparable compensation data to assist them in the critical decisions involved in attracting, motivating and retaining key executives at private companies. As a result of the significant number of companies participating in the survey, we are able to present the correlation between executive compensation and a number of variables, including financing stage, company size both in terms of product stage and headcount, founder/non-founder status, industry segment and geography. We also provide a number of analytics on how organizations evolve with additional financing rounds, Boards of Directors compensation and make-up, and we take a granular look at company equity plans.

The survey data was collected between June and September of 2007. During this period venture capital investment in the sector has steadily increased and many new companies formed. As a result, our expectation is to continue to see increasing competition for executive talent, along with a corresponding up tick in compensation packages.

Our survey has evolved over the years based on input received directly from the industry, and our hope is to continuously improve the data so that we can best serve the needs of our collective clients in the Life Sciences industry. In that regard, we encourage readers of this publication to submit comments and suggestions to help us most efficiently and accurately present the compensation dynamics of the market. Suggestions and comments should be directed to Mike DiPierro of **J. Robert Scott** (mike.dipierro@fmr.com).

Lastly, we would like to express our gratitude to two individuals who continue to contribute greatly to our publication: Professor Brian Hall and Associate Professor Noam Wasserman of the **Harvard Business School**.



KEY:

Non-
Founder

Founder

Demographics of Respondent Population

- The survey was conducted between June and September 2007. Data was collected from more than 1,000 executives in 166 Life Sciences and Medical Device companies.
- This report provides an aggregation of the data as well as an examination of the population from a number of different perspectives, including: financing stage, founder status, geography, headcount, business segment and product stage.

Financing Rounds

- For analysis, the population was divided between companies that have raised one or fewer rounds of financing, two or three, and those that have raised four or more rounds of financing. Companies in the earliest stage represent 24% of the population, those with two or three rounds raised represent the largest slice, just over 50% of the overall companies, and those with four or more rounds raised comprise the remaining 25% of the population.

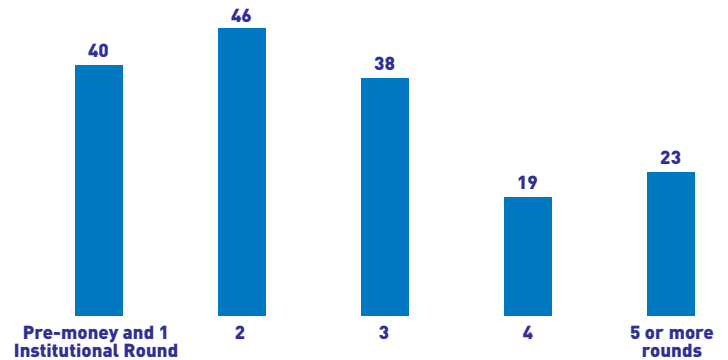
Founding Status

- 18% of the executives in the population were founders of their company. CEOs were most frequently founders with 43% having founded their company, followed by the CTO at 33% and President/COO and CSO/Head of Research and Development, each with 28% of the executives as founders.

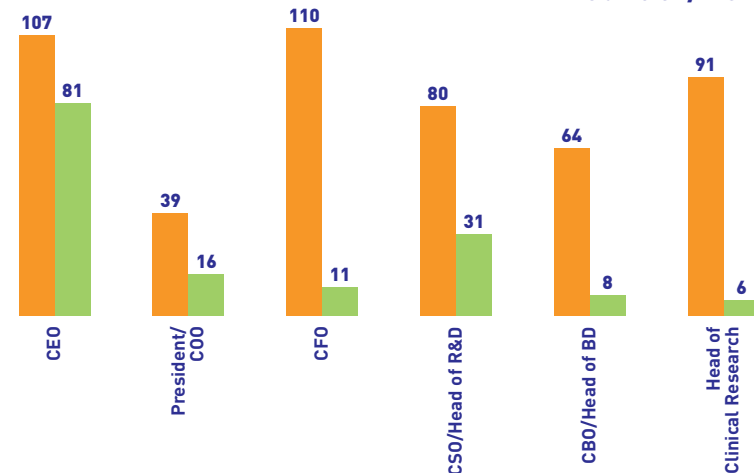
Headcount by Number of Full Time Employees (FTEs)

- 46% of companies surveyed in this report have fewer than 10 FTEs, while 17% were in the largest category, more than 41 FTEs. Responding companies continue to be in the early stages of growth.

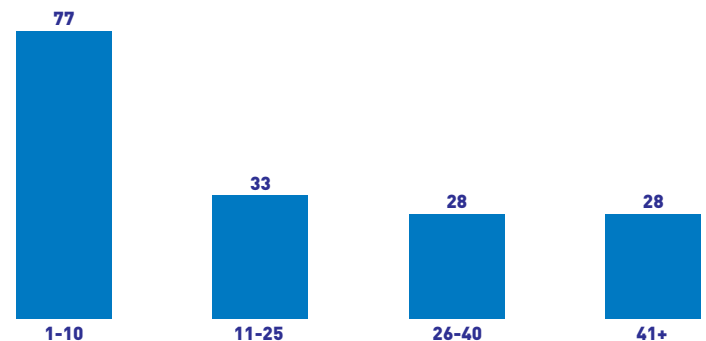
Financing Rounds



Founder/Non-



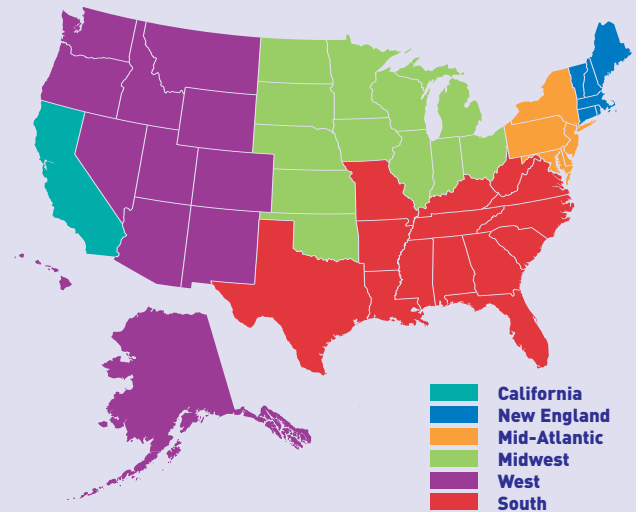
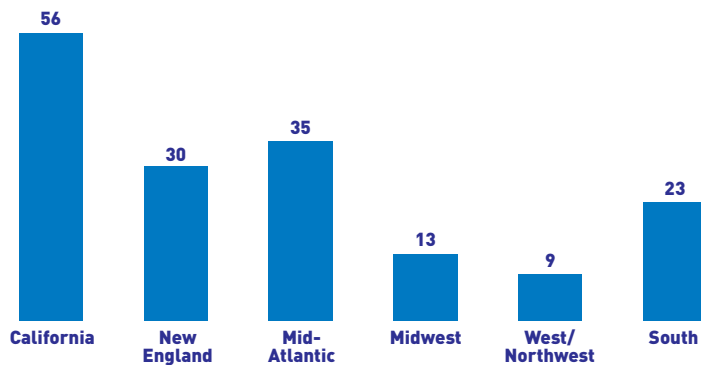
Headcount by Number of Full Time Employees (FTEs)



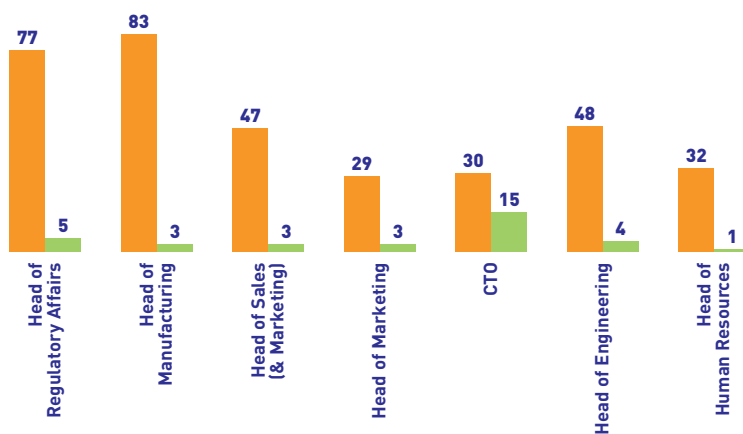


SUMMARY OF RESULTS

Geography



Founder Status



Geography

- The geographical distribution of the respondents was most concentrated in California, with 34% of the population, similar to previous years. The New England and Mid-Atlantic regions were the next largest regions with 18% and 21%, respectively. The geographical breakdown of the population closely mirrors venture funding trends in the United States.

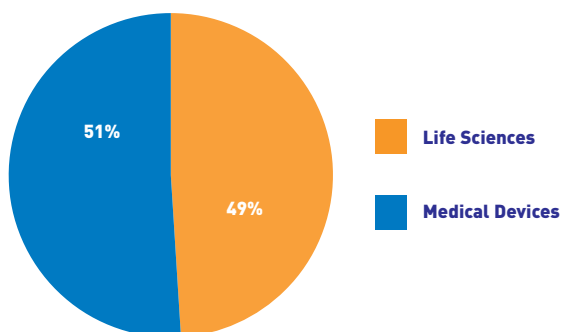
Business Segment

- Distribution between Life Sciences and Medical Device companies was closer than in previous editions of the report, with Life Sciences comprising 49% of the companies surveyed and Medical Devices making up 51%.

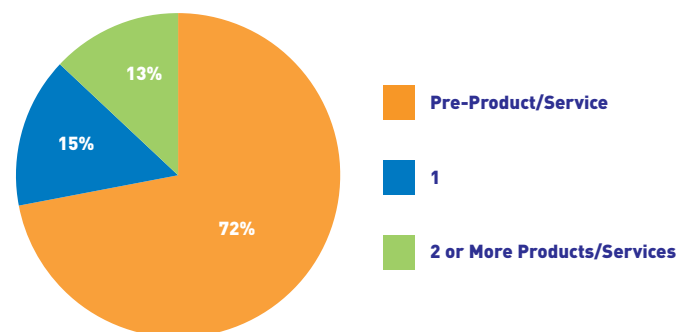
Product Stage

- 28% of the companies surveyed in this report currently have a product or service on the market.

Business Segment



Product Stage



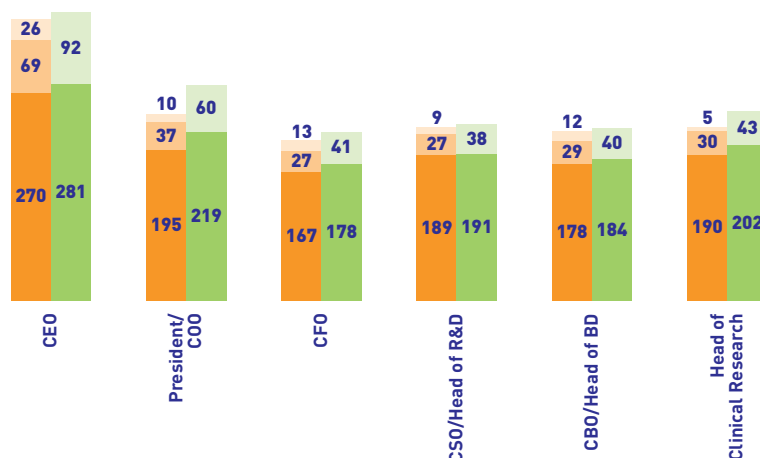


KEY:	2006	Target Bonus Not Received	2007	Target Bonus
	2006	Actual Bonus Received	2007	Base Salary
	2006	Base Salary	2007	Base Salary

Total Cash Compensation – 2006 and 2007

- This data represents 2006 and 2007 total cash compensation for non-founding executives. 2006 figures represent both actual bonus received and total target bonus for the year. 2007 bonus figures reflect target bonuses for this year.
- The total average rise in base salary across all of the positions surveyed was 5.9% from 2006 to 2007.
- The one position which saw a decrease in base salary was the CTO, dropping to an average of \$179,000 in 2007 from \$183,000 in 2006.
- The non-founder CEO experienced a 3.9% rise in base salary from an average of \$270,000 in 2006 to \$281,000 in 2007.

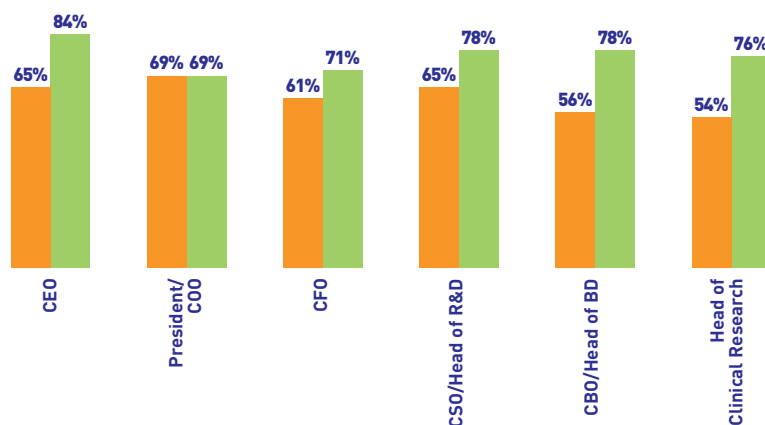
Total Cash Compensation



Executives Eligible for Bonus

- Not surprisingly, in 2007, the positions that are most frequently slated to receive a bonus are the Head of Engineering, Head of Sales and the CEO, with 92%, 89% and 84% of non-founding executives eligible.
- In aggregate, the number of executives eligible for bonus rose from 62% in 2006 to 78% in 2007.

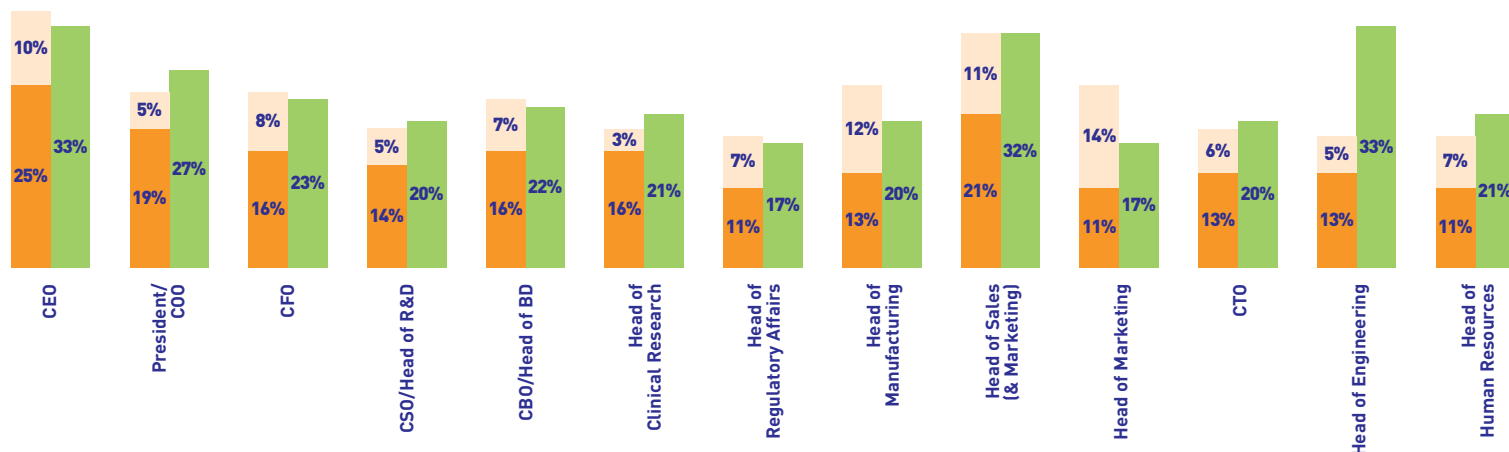
Executives Eligible



Bonus as a Percentage of Base Salary

- In 2006, the actual bonus paid to the CEO was 25% of base salary, highest among the positions surveyed.
- 2007 target bonus is again highest for the CEO with the Head of Sales not far behind at approximately one-third of base salary.
- Overall bonus targets as a percentage of base salary did not change materially from 2006 to 2007.

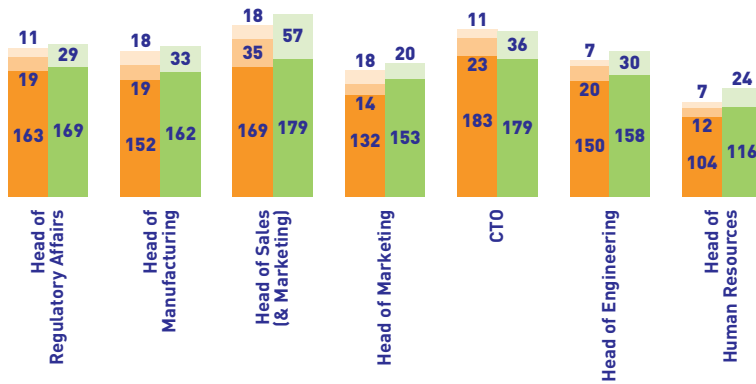
Bonus as a Percentage of Base Salary – 2006 and 2007



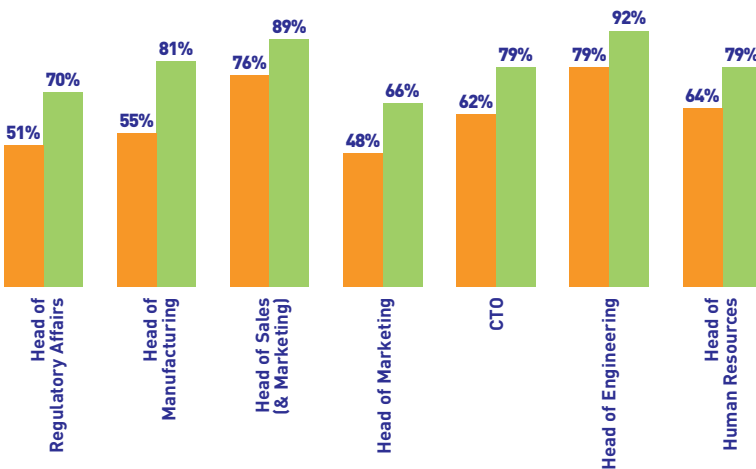


SUMMARY OF RESULTS

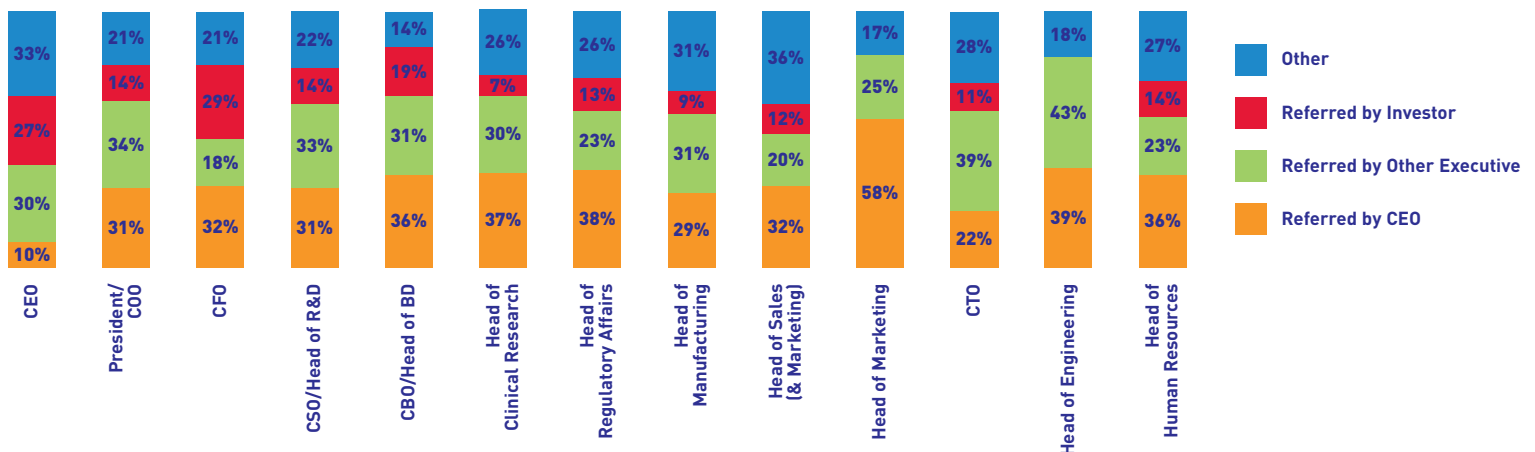
– 2006 and 2007



for Bonus 2007



Where Companies Locate Talent





KEY:

Median

Average

Current Equity Holdings

- Equity data represents fully diluted holdings for non-founding executives.
- Total average equity holdings across the 13 executive positions surveyed represents 18.08% of the fully diluted company, an increase from our 2006 report at 16.20%.
- Non-founding CEOs hold an average of 5.48% of their companies. At the median, 5.00% continues to be the norm.
- The majority of the executive positions surveyed hold an average of approximately 1.00% of their companies.

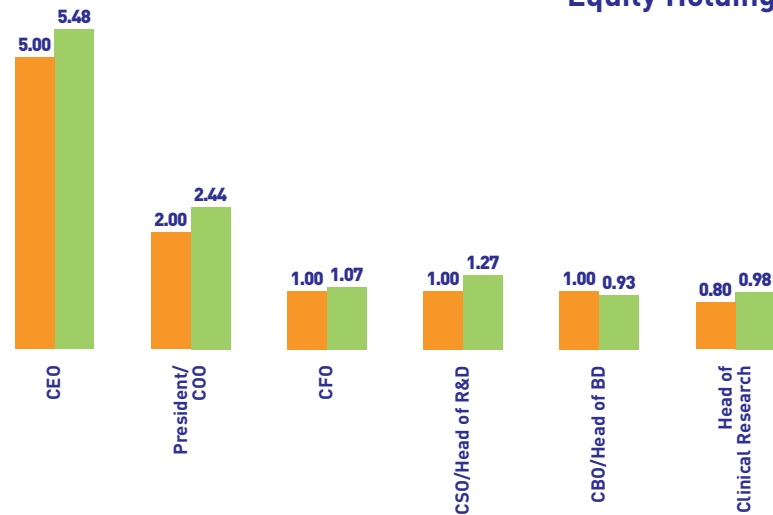
Equity Granted at Time of Hire

- Equity grants at time of hire were highest for the CEO, 5.97% at the average, and the President/COO with 2.87% at the average.
- 64% of companies surveyed utilize only options, while 17% use either restricted or common stock.

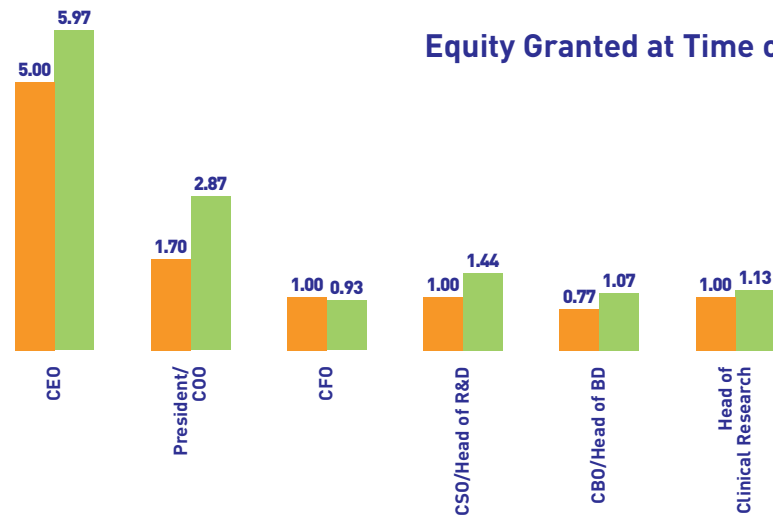
Severance Packages

- 72% of the non-founding CEOs in the survey have a severance package, with a median of 12 months, similar to previous years. Outside the CEO and President/COO, the non-founding executive team holds a severance package between one-third and one-half of the time.
- Severance packages are most often set at 6 months for the management team surveyed.

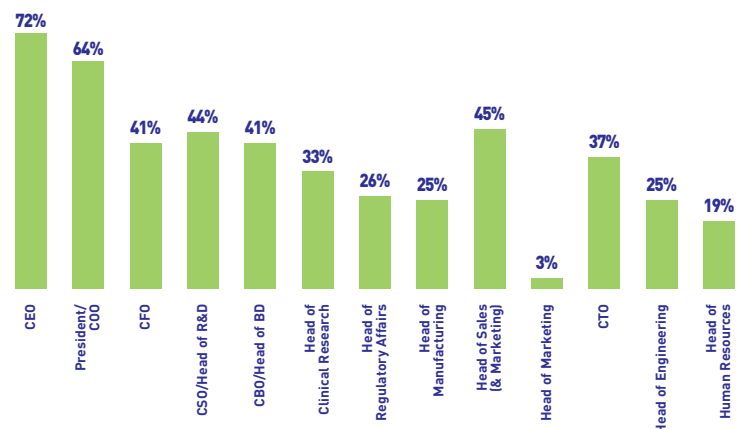
Equity Holdings



Equity Granted at Time of Hire



Executives with Severance Package

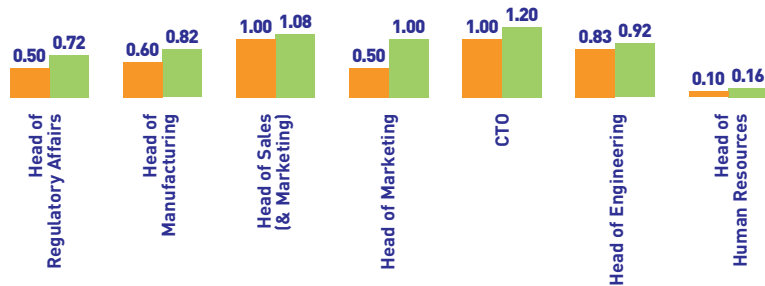




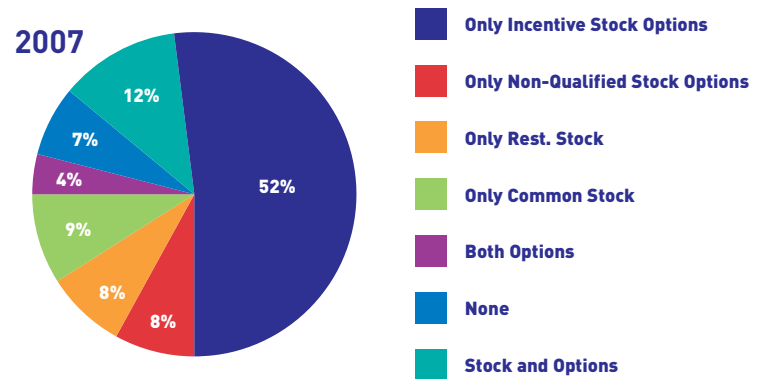
SUMMARY OF RESULTS

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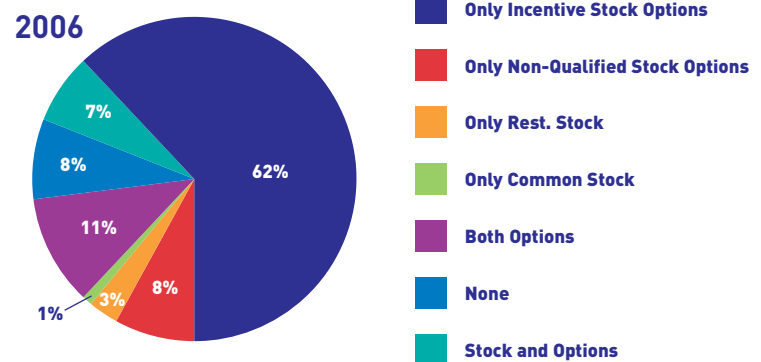
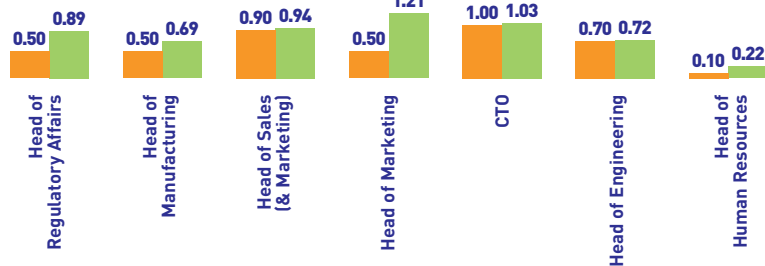
Median vs. Average (%)



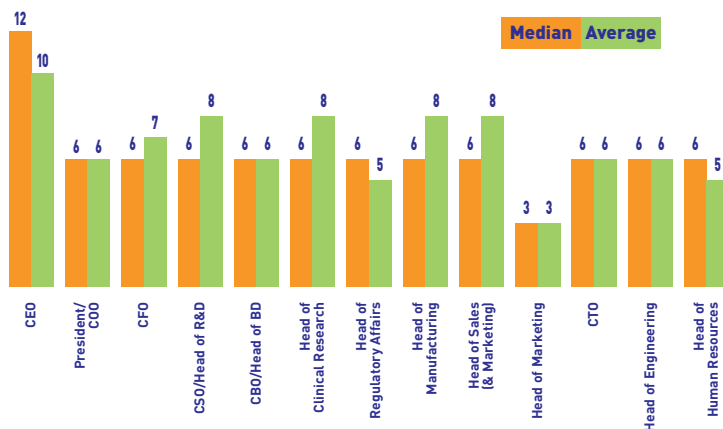
Equity Vehicles Used

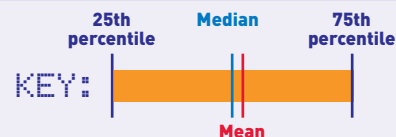


Hire Median vs. Average (%)



Severance Package (Median vs. Average in # of Months)





Total Cash Compensation

- Founding executives in the 2007 report saw a slight rise in average total cash compensation. For the founding CEO, base salary rose 7.3% to \$257,000. Target bonuses are also up for CEOs in 2007.
- In general, founding executives earn less than their non-founder counterparts, particularly in terms of average base salary.
- For the CEO, this difference is quite pronounced. A non-founding CEO commands a 10% premium over the founding CEO, \$281,000 for the non-founder versus \$257,000 for the founder.

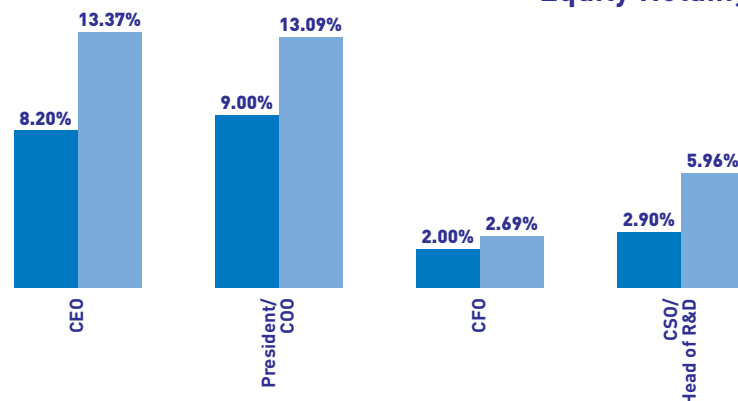
Equity Holdings

- As expected, founders hold a considerably larger equity stake in their companies than any non-founding executive.
- For the founding CEO, the average equity holding is 13.37% while the median amount is 8.20%. This difference is attributable to a small number of CEOs holding a relatively large amount of equity in comparison with other founding CEOs.

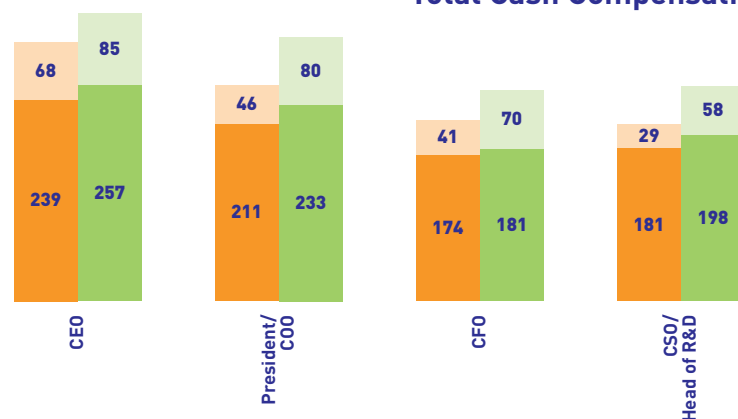
CEO Equity Holdings by Financing Round

- Dilution of equity for the founding CEO is consistent across rounds of financing raised, moving from an average of 17.70% at companies with one or fewer rounds raised to 8.06% at companies with four or more rounds of financing.

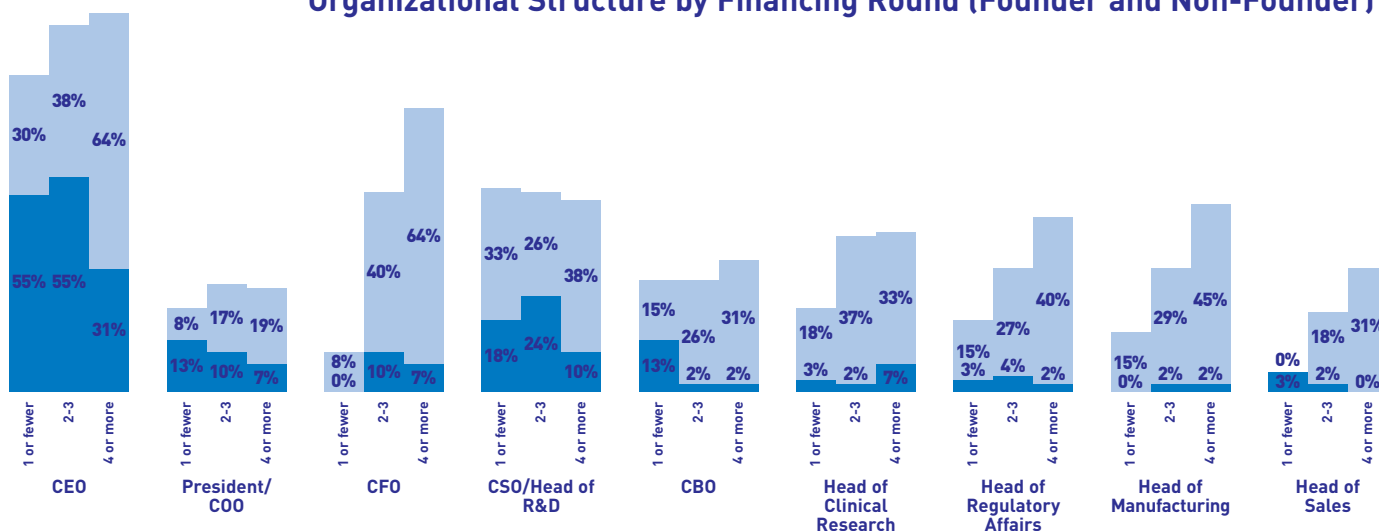
Equity Holdings



Total Cash Compensation



Organizational Structure by Financing Round (Founder and Non-Founder)



KEY: 2006 2007 Bonus
2006 2007 Base



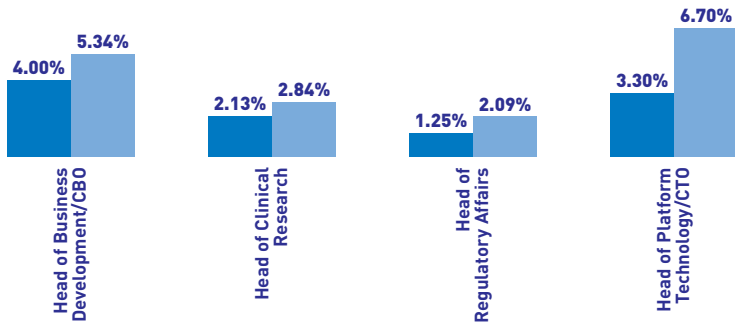
FOUNDERS

– Founders

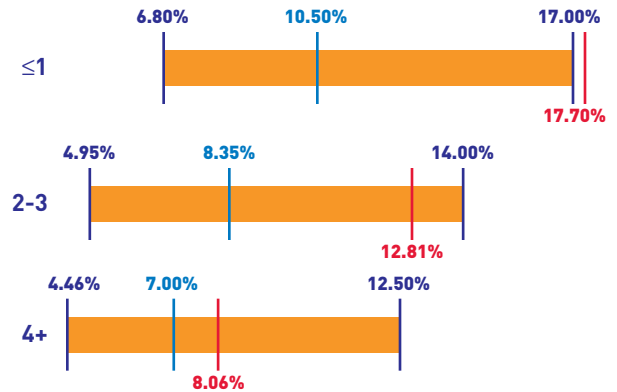
KEY:

Median

Average



Chief Executive Officer – Founder Equity Holdings



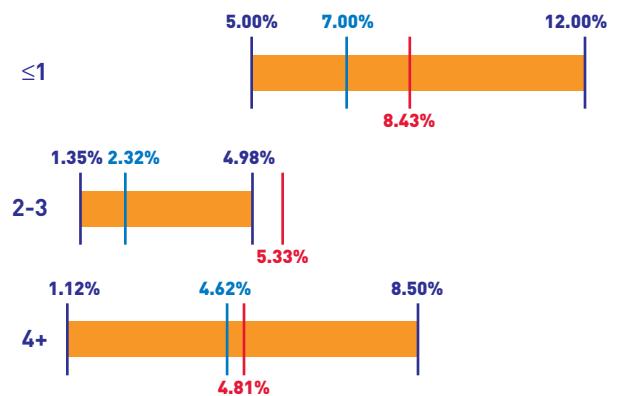
– Founders



President/COO – Founder Equity Holdings



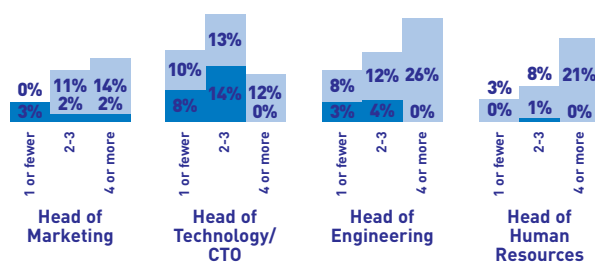
CSO/Head of R&D – Founder Equity Holdings



KEY:

Founder

Non-Founder





STANLEY N. LAPIDUS

Chairman of the Board, Chief Executive Officer HELICOS BIOSCIENCES CORPORATION

Mr. Lapidus is Chairman of the Board, Chief Executive Officer of Helicos BioSciences Corporation. He is a co-founder of Helicos BioSciences and has served as President and Chief Executive Officer since October 2003. Mr. Lapidus served as a Venture Partner at Flagship Ventures from March 2002 through September 2003. Mr. Lapidus founded EXACT Sciences Corporation in 1995, where he served as President from 1995 through 2000 and Chairman from 2000 through 2005. Prior to EXACT Sciences, Mr. Lapidus founded Cytoc Corporation, where he served as President from 1987 to 1994. Mr. Lapidus also holds academic appointments in the Pathology Department at Tufts University Medical School and Massachusetts Institute of Technology's Sloan School of Management. He earned a BSEE from Cooper Union. He has served as a trustee of Cooper Union since 2002. Mr. Lapidus is named as an inventor on 30 issued U.S. patents.

Bruce: Perhaps you could begin by discussing the formal academic training you received and how that played a role, if any, in becoming an entrepreneur.

Stan: I went to Cooper Union, a college in Manhattan, which did a great deal for me in three areas. First, it gave me an education. You can't invent without a modicum of physics and math. Secondly, it gave me a sense of myself as a competitive person. Thirdly, I developed the self-confidence to say I could solve problems often by coming up with novel ways to formulate the question. What an inventor does is come up with a new way to state an existing problem.

Bruce: Peter Cooper, the founder of your college, was a renowned and accomplished inventor. Given the technical orientation of the school, you must have had at least some idea or hope in your youth that your career would involve inventing.

Stan: I went to the Bronx High School of Science and graduated in 1966. Two of my classmates have won Nobel Prizes. I, myself, was an extraordinarily undistinguished student. What I really remember, however, is how smart my classmates were and how the thousand of us collectively were driven. I also remember vividly that a vast majority of our teachers were uncaring and unaccomplished. That said, there were a handful of exceptional teachers, particularly those in the Math and English departments. Then and now, we teach science to high school students merely as the memorization of disconnected facts. We teach nothing about the joy of discovery and, as a result, turn off many of our brightest young people to careers in science and engineering. You can't be a thoughtful and informed citizen in a civil society in the twenty-first century without being knowledgeable about the fundamentals of science.

Bruce: It sounds as though you were engaged as much by the humanities as the natural sciences in high school.

Stan: Your statement hints at one of the fundamental problems with education in the West. The idea that one can be an educated person with only a background in the humanities or the sciences is nuts. Our best thinkers, the people who change the world, were, and still are, men and women deeply steeped in both the sciences and the humanities. The idea that we educate undergraduates and

STAN LAPIDUS, CHAIRMAN & CEO, HELICOS BIOSCIENCES CORPORATION

award a BS or BA degree instead of a bachelor of science and arts is a great failing of the West's educational paradigm. Scientists must have a sense of the history of civilization and how science has been used and misused by governments. Non-scientists must be knowledgeable about the basic 'operating systems' of our physical and biological world.

Bruce: Before we get into a discussion about the companies that you started, I understand that you are now an instructor yourself. Is this your attempt to help correct a flawed system?

Stan: No, because the major flaws in educational systems in the West have to do with the approaches of teaching at the high school and undergraduate level. I teach graduate courses at MIT—without an advanced degree, yet wouldn't be allowed to teach at my local high school. MIT doesn't seem to care about the advanced degree or my teaching qualifications, but my local high school is concerned that I don't have a teaching certification. What connection does the teaching certification have to do with the quality of education? None. People come from all over the world to go to our universities and graduate schools. No one comes from all over the world to go to our public high schools.

Bruce: How did you begin your career after graduating from Cooper Union?

Stan: I've always been fascinated by the application of technologies to problems in medicine. I spent the first four years of my career working at Elscint, a medical imaging company in Israel, but my employment at Raytheon upon my return to the States most strongly defined what I was to become. I joined Raytheon's medical products division, which was developing an instrument called a gamma camera, constructed of a large scintillation crystal and an array of photo-multiplier tubes. Gamma cameras are used for identifying tumors in bone and in soft tissue by imaging where radiation localizes in a patient in whom radioisotopes have been administered. The isotopes concentrate in regions of higher metabolism which are seen as hot spots by the gamma camera, indicating a tumor. The core gamma camera invention was worked out in the 1950s, but the engineering problem we encountered at Raytheon was how to balance the large number of photomultiplier tubes. Over the years, the number of tubes increased from seven

to ninety-one. Raytheon was pioneering the ninety-one tube camera. One could balance seven tubes pretty easily in about fifteen minutes, but one simply could not balance ninety-one. Raytheon had bet a lot on this camera and found they could not get the tubes to be stable in production. I joined just as the first cameras were to be shipped and they just weren't working well. I must say that I had no idea, myself, how to improve the stability of the camera at the level of device physics. Raytheon's medical business was headed into a "crack-up."

Bruce: So, how did you come up with a solution?

Stan: As I mentioned before, I was confident with my ability to reformulate the question. I knew how to measure the instability of the photomultiplier tubes—easy to do. We used the measured instability data to calibrate out the non-uniformity. This was important because each of the ninety-one photo multiplier tubes was about the size of a tumor. If one tube was too "hot" or too "cold", a physician could misidentify an imbalanced photomultiplier tube as a tumor. Simply by illuminating the gamma camera with a uniform field of radiation, looking for "hot" and "cold" spots and applying the measured non-uniformity as an inverse correction factor allowed for an apparently perfectly uniform response from an imperfect instrument.

Bruce: As an engineer, this must have been a very pleasing outcome for you. Yet history tells us that you did not stay at Raytheon long after the advancement was made.

Stan: That was the first experience I had at patenting. It was also the first experience I had with the – not to be crass – "what's in it for me" aspect. The sales of the nuclear medicine business doubled the next year; a nice outcome for Raytheon. I got a \$100 check for inventing our way out of failure. Raytheon was an excellent company with excellent people. I got a paycheck whether I was inventive or not, but with no real upside. I decided it wasn't the value proposition I was looking for so I started to think about what life would be like as a guy who signs his own paychecks.



BRUCE R. RYCHLIK

Managing Director

J. Robert Scott

Bruce Rychlik has spent his entire career with J. Robert Scott, joining the firm in 1990. Bruce's practice focuses on recruiting Chief Executive Officers as well as functional leaders for primarily venture-backed Life Science companies including Chief Scientific, Technical, Medical, Financial and Business Officers at a national level.

Bruce has also recruited extensively in the Life Sciences for Corporate Boards, for Academic/Research Institutions in the area of Technology Transfer and for Global Health NGOs. In his career, he has also worked on numerous international recruiting projects throughout Asia, particularly Japan, as well as Europe.

In addition, Bruce spearheads the production of the Compensation and Entrepreneurship Report in Life Sciences, an annual study of executive cash and equity compensation for private, venture capital backed technology companies, done in collaboration with Harvard Business School, Ernst & Young and WilmerHale. He also serves as an Advisor to Convergence, an annual Life Sciences leaders forum.

Bruce earned an MBA from Boston University (1997) and a BA in Political Science from Dickinson College in Carlisle, Pennsylvania (1989).

Bruce: What was your chosen path to un-tethered independence?

Stan: I formed a contract engineering business with a college buddy of mine and an industrial machine vision company grew out of that called Itran. It was a company that did well enough to stay in business but didn't make a lot of money for its venture capital investors. However, two of the investors approached me and said, "Good run, could have been better; could have been a whole lot worse, too. Here is \$200,000. See if you come up with any other ideas that we like and we will invest some more." So, I set out to focus on important unsolved problems and began a semi-systematic look at problems that would involve image analysis (something I knew about), ideally with medical applications. I wound up cold-calling an individual at a clinical laboratory in Cambridge, Massachusetts and pitched him on a particular idea I had. He had no interest, but thought we could apply our knowledge of image processing with computers to the Pap smear. I didn't know what a Pap smear was but, based on his suggestion, that became the starting point of Cytyc.

Bruce: Did the idea of developing an alternative screening tool for cervical cancer, what Cytyc came to brand the ThinPrep test, come out of your market research and early engineering work?

Stan: Eventually it did. Fred Farber, who is now a senior executive at Idexx, and I spent much of the \$200,000 from the venture capitalists studying the market and developing the rudiments of the imaging technology. After considerable effort we could frequently find cancer, but we could not do it as well as trained technologists. So we decided to make a better Pap smear, rather than just read the existing, suboptimal smear. Having realized that we needed to make a better Pap smear, it took me about a millisecond to come up with the physical principles that we would use. After we built the first machines based on this invention, we discovered that the ThinPrep (as we ended up calling it) alone provided the benefit of increased accuracy that we had hoped we would achieve from the combination of an improved sample prep method and automated image analysis.

STAN LAPIDUS, CHAIRMAN & CEO, HELICOS BIOSCIENCES CORPORATION

Bruce: EXACT Sciences, your next company, makes screening technologies for use in the detection of colorectal cancer. Other than the indication, that sounds a lot like Cytyc.

Stan: We had done a fair number of small venture financings at Cytyc. Compared to other companies that were in the pathology or the clinical laboratory business, our valuations were consistently higher. At first, I thought that was because we were just better at this business stuff than others. Hubris knows no bounds! Then, of course, we realized that was not true. What we learned was that while we viewed ourselves as a pathology company, everyone else viewed us as a cancer prevention company or as a women's healthcare company. That was behind the higher valuations. I then started thinking about the idea of prevention for other forms of cancer. The most common cancer is lung cancer, but it was unclear that it could be prevented through early detection. Cancer life-tables showed that the second most common type of cancer is colorectal cancer, which was known to yield to early detection. We tried to create a ThinPrep for colorectal cancer at Cytyc but we could not get the technology to work so we set the idea aside. I picked it up later as a separate company which became EXACT. The path to commercialization through inclusion in practice guidelines, the Medicare approval process and reimbursement, is something that has turned out to be harder than we had estimated. When EXACT works that out, and it could be at any given time, I believe it will go through explosive growth.

Bruce: What did you learn from Cytyc that made you approach EXACT differently?

Stan: Getting out of the way sooner, which is to say looking for a successor earlier and hopefully before you demonstrate, ideally just to yourself, your total incompetence. You may never get the timing just right. There are some scientists/inventors/entrepreneurs who have become hugely successful. Bill Gates and Steve Jobs are two of them. For the rest of us, you have to know what you're good at, make sure that you hire the best possible successors, and then get out of the way in a more or less graceful way. If you are comfortable with yourself, then it's an easy thing to do. If not, then you wind up competing with the people that you hire and that is crazy. Second, we made sure that each financing at EXACT

was larger than comparable financing rounds at Cytyc. Third, I took more care in forming the board. We had a smaller board and we had no observers. That is the strongest advice I can give to any young man or woman starting a company; do not get snookered into having a large board or a board with lots of observers.

Bruce: Helicos, your most recent venture, is a company that is doing single molecule genetic analysis. What are you leveraging from the past in this venture or seeking to do that you have not done before?

Stan: I have never worked before on a technology that was so close to the cutting edge of science. The physics, chemistry, and engineering are all hard, but we have a fantastic team. At Cytyc, developing the ThinPrep was about applying well known principles of physics and engineering to a cool gizmo that solved a heretofore improperly addressed problem. At EXACT, the challenge was to apply known principles of molecular biology in a novel way. Helicos is more of a swing for the fences in the sense that we believe our lead product, the HeliScope, will become a central force in the unraveling of the mysteries of genetic diseases. Our value proposition is creating tools that revolutionize an understanding of the molecular basis of cancer and other diseases. The result will be new methods to develop drugs and better methods to diagnose the diseases that account for the vast majority of mortality in Western mankind.

Bruce: You have been a broad proponent of venture capital in terms of financing Cytyc, EXACT, and Helicos. Did you ever consider other options when forming these companies?

Stan: I do not want other options for financing. Venture investors make for good companies. I would not want to staff a board with friends, and I would not want to staff a board with angel investors, though it is true that some angel investors themselves are successful business people. I really do like professional investors. I like people who spend their time thinking about how you build value in small companies, how you round out teams, and how you position a company in the market. Raising venture capital makes you think your story through. Your business vision is often more clear at the end of a fund-raising round than at the beginning because of the tough questions VC's ask. For investors, I look for



individuals who are really good strategic thinkers, who have really good Rolodexes, and who have reputations for integrity and for playing well with others. You will also notice that each of these companies have gone public. I have always seen an IPO as a necessary, but not sufficient condition, for liquidity. For some of my venture investors in the past this was different, it was a liquidity event. For management it is not. An IPO just raises the hurdle of performance.

Bruce: Does Cytoc's recent sale come as a surprise to you some twenty years after you founded it?

Stan: It was a surprise that Cytoc recently sold for \$6 billion, a market capitalization that very few medical device companies have reached. When I started the company, the idea that Cytoc would actually achieve \$100's of millions in sales and reach a market capitalization of billions of dollars was beyond my wildest expectations. But Pat Sullivan, my successor as CEO, is an extraordinary guy and Cytoc had, at its foundation, an extraordinary market, value proposition, and technology. That was a very good combination. To the extent that I am a small player in the company's success is because I had identified the Pap smear as a medically important backwater that had the potential of being a \$500 million or \$1 billion opportunity. With a thoughtful marketing program to the public and to the medical pathology communities, Cytoc rebranded the Pap smear and turned it from a loss leader to a diagnostic which, in Pat's hands, had a greater than 80% gross margin. Because the value of an improved Pap smear was underappreciated by the existing players in the diagnostics business, Cytoc had a great ride. We had no competitors among the established diagnostics players. They were not interested in the Pap smear and thought I was nuts for pursuing it.

Bruce: Does it surprise you now, twenty-five years or so after the formation of Amgen and Cytoc, sitting in Kendall Square in Cambridge at Helicos, that the likes of Novartis among others, are in your midst? Is this "big pharma" and "big biotech" coming back to the city?

Stan: I am astonished! I never would have guessed. In the 1960's young men and women went to college in a city then went to work in a suburb. That was viewed as the natural progression of life.

STAN LAPIDUS, CHAIRMAN & CEO, HELICOS BIOSCIENCES CORPORATION

Now our graduates from schools here quite reasonably expect to live their professional lives within a bike ride, a T ride, or a walk away from work. Bravo! Itran, the engineering company I started, was in New Hampshire where the people we needed were a short commute away. It is difficult to start a biotech company in New Hampshire because the life science community is truly centered around places like Harvard, MIT, Tufts, and BU. The negatives of being “in town” are that Boston and Cambridge have high rents for industrial space and high costs of housing. They also have the kind of primary and secondary schools that are either barely adequate or that make you want to send your kids to private school. As positives, we have great universities. We have four medical schools, including UMass Medical. We have zillions of post-docs. We also have the social and diverse cultural infrastructure that brings people from all over the world to want to work here. At Helicos, our scientific staff and our commercial team are every color of the rainbow and from every ethnic background. We are all drawn to the Boston area since very few of our team are native to New England.

Bruce: You have largely kept focused on instrumentation and diagnostic throughout your career. Have you ever been lured to seriously consider therapeutics? Are you already thinking about company number five?

Stan: When I was at Flagship as a venture partner, I took a serious look at two therapeutic opportunities. For reasons that did not have to do with the underlying science, they were not the right things for me to do. I certainly have the confidence to start a therapeutics company. But right now, I am not thinking about company number five. I am fully focused on Helicos.

INTERVIEWS



R. SANDERS WILLIAMS, M.D.

R. Sanders “Sandy” Williams, M.D., is dean of the Duke University School of Medicine and vice chancellor for academic affairs at Duke University Medical Center.

Dr. Williams is a practicing cardiologist and researcher. Prior to his appointment at Duke, he was Chief of the division of cardiology and Director of the Ryburn Center for Molecular Cardiology at the University of Texas Southwestern Medical Center in Dallas. A graduate of Princeton University and Duke University Medical School, Dr. Williams did his residency at Massachusetts General Hospital and completed a fellowship in cardiology at Duke University. He served on the Duke University School of Medicine faculty for nine years.

Dr. Williams has published more than 150 medical and scientific articles and holds five patents for his work.

Interview: Bill Holodnak (BH), Jonathan Fortescue (JF) – J. Robert Scott; and Dr. Sandy Williams (SW) - Duke

BH: Your career is marked by elevated and richly variegated accomplishments as a physician, scientist, and educator. Tell us how it all got started.

SW: My path has been unusual with some very surprising twists and turns. Upon entering college, my career interest was reflected in an international affairs major. The thought at the time was that I might enter the Foreign Service or perhaps become Secretary of State. Things changed junior year with a biology course taken as an elective. This was at the dawn of the molecular biology era. Marshall Nirenberg had just cracked the genetic code the year before. My own very inspiring biology teacher breathed life into the structure of DNA and proteins. Some instinct was triggered that caused me to claim this new field as my future. While completing my degree in international affairs, I took science courses sufficient to apply and be accepted to medical school. At the time, this academic history made me a very unusual applicant, but several schools were encouraged by my maverick approach.

While matriculating in medical school, I was a bit – actually I was quite – naïve compared to many of my fellow students who came with more conventional pre-med experience. What seemed old hat to many of them appeared new and exciting to me. The subject matter of my first year biochemistry course felt to me like looking at the Sistine Chapel. It was so beautiful the way metabolism worked and things fit together in our cells. This aesthetic perspective provided inspiration to do research about the inner workings of cells and molecules, along with fuelling an idealistic urge to help patients. Together, these forces drew me toward the career of a physician scientist.

BH: Did you have an intermediary goal ... to become an orthopedic surgeon or a neurologist? Or did your enthusiasm very quickly morph into a scientific vocation?

SW: For the first ten or so years of my career, I was more physician than scientist. As I got more deeply into the science, research began to dominate my ambition. The second ten years or so of my career emphasized science. In my third and current phase, I have come to focus more on issues of organizational leadership, even

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though I still like being a doctor and a scientist. My approach to medicine has always been to ask questions with the underlying biology in mind. This attitude also pervades my teaching. I urge medical students today to think of themselves first as biologists and only then as physicians. My conviction is that such an attitude makes for a better physician.

JF: It has been said that the Dean of a Medical School is an “impossible job.” How did you wind up moving along the administrative path? And has this third phase in your career in fact been an impossible job?

SW: It is “impossible” to have the number of contacts that you would like to have with faculty and students but, on the other hand, it is a very rewarding job. I think that my transition to a leadership role came in steps. First, I became the director of a cardiology division and a cardiovascular research center. During this period, I was still very active as both a physician and a scientist, but I liked the leadership part and helping others to advance their careers and having some ability to adjust the environment to help people live up to their potential. Moving to a deanship is a more dramatic step, in that the job is no longer just about you as a physician or scientist, it is about what you can do to structure an environment in which the trainees and the faculty can achieve at the highest level.

BH: In terms of structuring that productive environment, does fundraising constitute the dominant “note in the chord” or must you address other realities - culture creation or cultural enhancement, optional organizational structure, that sort of thing?

SW: Fundraising is an important part of senior leadership in any academic medical center, but by no means represents the defining element of leadership. There are hundreds of small decisions and scores of quite major decisions that are addressed with the dean which, over time, aggregate and can produce quite different organizational and operational outcomes. A multitude of decisions add up to shape a school over a decade. Each dean clearly has an opportunity to put a lasting stamp on his/her institution.

BH: Once you got involved in administration or leadership, how did you engage in or become engaged by entrepreneurial initiatives?

SW: I think the term “entrepreneurialism” as it applies to academic medicine has at least two dimensions. The first is entrepreneurialism that results in scientific creativity or educational productivity, as opposed to financial return. I like to think of myself as consistently nimble when recruiting faculty and in trying to educate our students and residents in the best light. The other meaning of entrepreneurialism is the more traditional use as it concerns business. Academic medical centers are a potent source of the ideas that foster novel medical technology. Just as pure scientific discovery and the education of the physicians and scientists of the future are part of our mission, so too is making knowledge practical. For a technology to reach patients and the public, it has to involve business at some point. So, universities and academic medical centers should be places where that type of interaction is up front and center, as well. At Duke, we pride ourselves as being entrepreneurs across that entire spectrum from discovery to the marketplace.

BH: Who were the most influential mentors in your career? Who helped to inspire you?

SW: One was Bob Lefkowitz, the great scientist who discovered the seven membrane spanning receptor super family. Bob has been entrepreneurial primarily in his research but his efforts also have empowered a lot of drug discovery and technology development. Another mentor was Andy Wallace who was part of the team that first developed heart surgery for the treatment of cardiac arrhythmias which later spawned the entire field of invasive electrophysiology. Andy was also entrepreneurial as an educator and later became a dean and did that very successfully. Mike Brown and Joel Goldstein are heroes to many physicians and scientists, but I had a chance to work closely with them in my years at UT-Southwestern in Dallas. They not only set the standard of how science should be done, but also how science and its service to society can cross over into the biotechnology and pharmaceutical industries. Their work has led to substantial technological innovation. The other person who is a close personal friend is Lewis “Rusty” Williams. Rusty (a Duke alum, by the way) developed an extremely distinguished career as an academic scientist and then moved into industry, first with Chiron and now with his own company, FivePrime Therapeutics. Rusty is a restless spirit – he has always been out front in his ideas and resolutely disinclined to accept conventional wisdom or authority in almost any dimension.

INTERVIEWS

**WILLIAM HOLODNAK**

William A. Holodnak is Founder and President of J. Robert Scott. In addition to managing the firm since its inception in 1986, Bill conducts senior level search assignments in a variety of industries including For-Profit Education, Biotechnology, Medical Devices, Financial Services, and Technology. His practice emphasizes assignments for Chief Executive Officers and Members of the Board of Directors.

Prior to joining J. Robert Scott, Bill was a Vice President of a retainer-based executive search firm which serviced the Venture Capital and High Technology industries on a national basis. Previously, he was a member of the professional audit staff of PricewaterhouseCoopers' Boston office and holds a CPA certificate in Massachusetts. Before joining PWC, Bill successfully managed the Brattle Theatre in Cambridge, Massachusetts.

Bill holds an MBA from Boston University (1976) as well as a graduate degree in Medieval History from The Johns Hopkins University (1971). His undergraduate degree is from Canisius College (1968) in New York. He has taught courses in History and Film Criticism at both Johns Hopkins and Boston University respectively. He has spoken at Harvard Business School, Northeastern University, Babson College and Boston University on organizational development, succession planning and career management. Bill is a Trustee of the Berklee College of Music and Chairs the Membership Committee and serves as an Advisor to the Harvard-MIT Division of Health Sciences and Technology.

Bill is married with two children, Lili, a graduate of Princeton University and the creative writing program at Boston University, and John, a graduate of Amherst College.

BH: Let's talk a little bit about Duke now. This is a great educational institution which has been very innovative in trying to bridge the gap between the laboratory and the marketplace and in finding creative ways to make these things happen and get them funded. Where does that impulse come from and how much does Duke's reputation for creativity reflect your own contribution?

SW: I was attracted to Duke for medical school in part because I sensed this entrepreneurial spirit. There was a brashness to it ... a sense of adventure that the place emanated and that I recognized even in my very naïve state as a college senior. Duke had an innovative curriculum then - as it does now. We are the only school that affords students a full year of independent research in a four year medical school curriculum, kind of a mini PhD as part of the MD. That attracted me and continues to attract students who want that kind of deep dive into a specific area of medical science, as opposed to the broad knowledge that medical education more generally entails. What I tell the current Duke students about the value of that third year of research is that it offers the chance to become the world's expert in something.

At Duke, we value equally the achievements across the spectrum from scientific discovery to translating that work into something useful and then actually gathering the evidence from clinical research. We also pride ourselves on having the right kind of academic industry relationships and presenting user friendly interface to industry partners, while at the same time being clear about the ethical standards that each side must maintain. Companies have fiduciary responsibilities to shareholders; universities do not. We have a different kind of fiduciary obligation but, nevertheless, there can be areas of great mutual interest and mutual benefit when academic/industry partnerships are done right. Such activities can be very healthy and good for society. We like to think of Duke as a place where they can be done often and well.

BH: The Duke Translational Research Institute would seem to typify what you are describing here. How did that entity come into being and what is its future?

SW: Let me make a brief aside. We have a still relatively new President of the University at Duke in Richard Brodhead and a still relatively new Chancellor of the Health Sciences in Victor Dzau. When they came to Duke, both were struck by the fact that there is

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a different ethos here; there is a higher calling given to this translation of knowledge into something useful for society. Both picked up on this as being consistent with their own values and achievement and saw the opportunity to emphasize it even further at Duke. Their institutional entrepreneurial spirit is an important part of their being in Durham.

From this ethos came a series of new organizational entities—the Duke Translational Medicine Institute (DTMI) being the largest and most pervasive of these. It is built on the foundation of the Duke Clinical Research Institute (DCRI) which is, without question, the premier academic clinical research organization in the world. DCRI is known for its creative study design and for the veracity of the evidence that is produced from clinical trials. DCRI has a large book of clinical trial business from both industry sponsors and from the NIH. As a sister to that very large and well developed entity, we also are building the Duke Translational Research Institute (DTRI) that now bridges discovery biology and clinical trials. This activity is organized and funded in ways that are more robust, systematic, and creative than anything we have done before. DTRI project teams include a business specialist and a clinical trial specialist; they concentrate on a novel device idea or promising compound and move it much further forward within the university before spinning it out to venture capital. In many ways, DTRI does what venture capital used to do in advancing the value of early stage medical technology.

There is a third leg of DTMI that we are quite proud of as well, which is Duke Community Research (DCR). DCR involves reaching out to our local community, to be sure that the research that we do is actually enhancing the health of our local community as well as capturing what can be done well for the local citizens who are research subjects. The NIH peer reviewers like the way we have put the three legs of DTMI together and have given us the number one score in the country when we proposed this for federal funding as part of the NIH roadmap. This led to Duke's receiving one of the first CTSA grants from the NIH for \$52.7 million.

BH: Is there any tension at Duke over the possibility of your faculty having personal, financial interests that are tied up with companies that grow out of research?

SW: We regard it as a healthy thing for faculty to have relationships with industry groups either as inventors, scientific consultants, or as board members, but some tensions are

inevitable as you suggest. We adamantly require faculty, every year or upon any substantial change, to disclose all such relationships which are then reviewed to determine any potential conflicts of interest. Occasionally, conflicts do arise, but the potential for conflict, in my mind, is no reason to categorically avoid such relationships. Overall, such tension is very healthy for the biomedical enterprise and generally has a salutary effect on the life of the institution.

BH: Is there any aspect of Duke's medical enterprise that causes you to lose sleep at night?

SW: What troubles me most is the future and the tenuous nature of the whole economic system that sustains academic medicine. We rest on pillars of federal policy decisions, largely around the NIH's budget and on societal decisions about how to compensate for medical care. Those are the primary income streams that have driven academic medicine for decades. Philanthropy comes in as an important piece, but the other two pieces are far and away more impactful.

BH: So the future of Duke depends upon successes like that of the DTMI. How do you feel Duke's efforts in this vein compare to those of your peer institutions? Do you feel that Duke is allied to places like Stanford and MIT in terms of a similar robust enthusiasm for technology transfer?

SW: The biotech industry developed more quickly in the Bay Area and Southern California and in Boston than it has here, but the Research Triangle Park is now fourth in the number of new company formations. There is a strong industry spirit here locally. Duke came to that part of the game somewhat later than our sister institutions, but now we are right there with them.

BH: Well, let's now go from the micro to the macro. We have talked about the good things happening in Northern Carolina. Why don't you comment a little about the globalization of academic research and, while you are at it, why don't you tell us a little bit about Duke in Singapore and why that represents particularly fortuitous access to the international arena?

SW: The globalization of academic medicine is proceeding rapidly. You can see increasing participation of laboratories outside the United States in the papers published in the leading journals and



JONATHAN FORTESCUE

Jonathan Fortescue joined J. Robert Scott after eight years at another executive search firm. His practice is national in scope and emphasizes leadership positions for clients who are creating new knowledge or working to shape the world, including major research universities, venture-backed life sciences companies, not-for-profit organizations, and government relations functions within larger organizations.

Prior to his career in executive search, Jonathan taught at Harvard for eleven years, first in the English department, where he was a perennial recipient of Derek Bok Distinguished Teaching Awards, and then in History and Literature where he won the Alan Heimert Teaching Prize. A scholar of American literature and culture, he wrote the introductions to and the literary chronologies for three of the eight volumes of the Cambridge History of American Literature. He was graduated with honors from the University of Massachusetts at Amherst with degrees in English and in Linguistics. A recipient of an Andrew W. Mellon Fellowship of the Humanities in 1989, he earned his M.A. and Ph.D. in English and American Literature and Language from Harvard University.

Jonathan lives with his wife Elizabeth, a cardiologist at Children's Hospital, and their son William in Wellesley, Massachusetts. Jonathan is also an avid runner with a personal best marathon time of 2:40:35.

in the papers presented at the leading international scientific societies. The US is still the premier site in the world for biomedical science, but the rest of the world is catching up quickly and the scale of investment being made in other countries, in some respects exceeds ours. The US is still a wonderful place to do research, and I am grateful for the public support we have, but we are now in a period of standstill with respect to the growth of the NIH budget. Other countries are not dependent on the NIH; this is leading trainees to look elsewhere for opportunity and it is even leading to senior investigators, in some cases, finding that there are more resources elsewhere. Duke's relationship with Singapore was a result of a recognition that, rather than watch these trends passively, we should look for partners with whom we can work well and toward a mutual benefit. So when Singapore approached us five years ago about a potential alliance, we were interested and negotiated for several years and signed a contract in 2005. Our venture there is now progressing beyond original expectations.

BH: How so?

SW: Well, let's go back to basics. Why would Duke want to commit time from its senior leadership, commit some of its faculty to relocate ... why would Duke see it as advantageous to have a partnership like we have in Singapore? First, we recognized that globalization of medicine is happening and happening in a big way. We would like students and faculty and other types of trainees to come to Duke because they believe we will provide a good grasp of what globalization means – where its dangers and advantages reside and how best to leverage that dynamic and potentially influence it. There are flows of people and ideas back and forth from Duke to Singapore and from Singapore and neighboring countries back to Duke all the time now. The second reason to be in Singapore is to make ourselves better. In the process, we have to refine our own curriculum, identify some areas of weakness that may not have been apparent and then strengthen ourselves in order to properly export this content. Our standards are now unequivocally global standards. The third reason is that, at a time when our growth domestically is limited, key programs at Duke saw mutually advantageous partnerships abroad. This is happening now in the Singapore project. I will give you two specific instances. We announced recently that Colin Blakemore, who is one of Britain's most distinguished neuroscientists and formerly the Head of the British Medical Research Council is coming to

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Singapore to join our medical school in partnership with the A-Star Research Institute on the island. We're in discussion now with four or five other very notable international neuroscientists to relocate there as part of a larger neurosciences initiative. Several Duke faculty members have moved either all or part of their research operations to Singapore and will benefit from the local resources. We now also have an initiative gearing up in infectious diseases. A similarly notable infectious disease specialist, Dr. Duane Gubler, also has become a Duke faculty member, both in the US and in Singapore, to lead a program that has a foot in Durham and a foot in Singapore. The tree will thus grow from two trunks.

JF: One of the issues around globalization is the risk inherent in cross-border enterprises. As you know, another fine institution, Johns Hopkins, ran into difficulty with Singapore. How are you managing that relationship between the Durham campus and the Singapore campus to ensure success?

SW: That's a good point. There is always risk in such complex ventures and I can't say that we've eliminated risk in this case. I do think, however, that we have developed a strong working relationship with our counterparts in Singapore with a high level of mutual trust. One of the things learned early on is that we need to be very explicit about what the expectations are from both sides. I think, problems arise – are more likely to arise – when there is a lack of real clarity over what each side is supposed to do. So we try to be extremely scrupulous about those expectations in Singapore and, so far, they have met all of our expectations and we have met all of their expectations. It's a happy marriage so far.

JF: Your career has in a way come full circle in that international politics are now an essential part of your medical considerations. In that vein, how do you view the future of medical education and what will be required of the next generation of leaders in medical education?

SW: I don't claim to have a crystal ball, but I'll share a few ideas. Number one, the knowledge base required to practice excellent medicine is expanding beyond the capability of the human mind to sort it. My belief is that medical education needs to increase the pace at which students learn to fluidly utilize information technologies. Rote memorization, except for the essential framework of

knowledge, is going to become a thing of the past. The use of information systems at the point of care will increasingly become what doctors do. The other trend is towards care delivered in teams as opposed to medicine as an individual craft. I think the average Medicare patient sees something like twelve to fourteen doctors a year, but our current systems aren't set up to facilitate that teamwork. Medical education needs to instill this sense of working collaboratively and medical practice organizations increasingly will need to become team-based enterprises. Finally, like many people, I have high hopes for the acceleration of molecular medicine. Thus, we believe a comprehensive grasp of the principles of cell and molecular biology are an important part of what good doctors need to know and that requirement is going to increase over time.

BH: How is your job going to change over the next decade? What kind of people are going to be drawn to leadership positions in academic medicine?

SW: I wouldn't want to be prescriptive about the kind of person who can lead successfully. The model we have at Duke for our medical leaders is that they need to be biologists and scientists with an underlying deep dedication to patient care. Those ingredients will continue to exist in our leaders, but they will also have to know how to manage increasingly large and complex organizations. I commented before about some of the healthy aspects of medical school faculty having contact with industry. This is true for me as well. From my own participation in industry related activities, I have learned a tremendous amount about management and how big organizations are led and moved and run successfully. For example, communications in those settings differ from the personal context that used to dominate the life of academic medical centers. Clearly, we will have to evolve to adapt their model. So, those are some of the trends that the next generation of leaders will have to deal with.

BH: Sandy, thanks so much for sharing your personal history, your experience at Duke, your views on the academic / commercial nexus, and globalization in the "industry" of medical research. Best wishes for continued success in meeting all of the stimulating challenges of your complex professional life.

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