

William Rastetter

*Interview conducted by
Matthew Shindell, Historian, UCSD
June 27, 2008*

SAN DIEGO TECHNOLOGY ARCHIVE



William Rastetter



Dr. William H. Rastetter, Bill, Ph.D., co-founded Receptos, Inc. in 2007 and has been its Executive Chairman since May 2009. Dr. Rastetter served as a Partner at Venrock which he joined in 2006 until 2013. Dr. Rastetter focused on biotechnology investments. He served as an Interim Chief Executive Officer of Receptos, Inc. from May 2009 to December 2, 2010. Dr. Rastetter served as the President and Chief Executive Officer at Biogen Idec Inc. from December 1986 to January 2002, the Chief Executive Officer from January 2002 to November 2003, the Chairman since 1986, a Director from 1986 to December 30, 2005, and served as an Executive Chairman. He served as the President at IDEC Pharmaceuticals Corp. from 1986 to 2002. Dr. Rastetter served as the Chief Financial Officer at IDEC Pharmaceuticals Corp. from December 1986 to November 2003, the Chairman from May 1996 to November 2003, and a Director of IDEC Pharmaceuticals Corp. since 1986. From 1984 to 1986, Dr. Rastetter was a Director of Corporate Ventures at Genentech Inc. and served in a scientific capacity at Genentech. He has been Non Executive Chairman of Illumina Inc. since January 2005. Dr. Rastetter has been the Chairman of Fate Therapeutics, Inc. since November 2011. He was an Interim Chief Executive Officer at Fate Therapeutics, Inc. until October 15, 2012. Dr. Rastetter joined Fate Therapeutics on December 14, 2011. He has been Chairman of Neurocrine Biosciences Inc. since May 25, 2011. He served as Executive Chairman of Biogen Idec Ma Inc. since December 31, 2005. He has been a Director of Illumina Inc. since November 1998. He has been a Director of Regulus Therapeutics Inc. since April 1, 2013. Dr. Rastetter serves as a Director of Argonaut Technologies Inc. and Neurocrine Biosciences Inc. since February 8, 2010. He has been Life Director at BIOCROM, Inc. since April 2007. He is a Board Member of the California Healthcare Institute. He served as a Director of Spiros Development Corp., since 1998. Dr. Rastetter served as a Director of the Biocatalysis group, and a Director of Chemical Sciences. As a Director of Corporate Ventures at Genentech Inc., he served as a Director of Spiros Development Corporation II Inc. and Spiros Development Corp. since 1998. Dr. Rastetter served on the Boards of Directors of Genentech's joint venture companies, Genencor (with

Corning and A.E. Staley), HP Genenchem (with Hewlett Packard), GLC Associates (with Lubrizol Corp.), and Travenol-Genentech Diagnostics (with Travenol Laboratories). From 1975 to 1982, Dr. Rastetter held various faculty positions at the Massachusetts Institute of Technology. He held various faculty positions at MIT, won the award for "Excellence in the Teaching of Chemistry" at Harvard, and is an Alfred P. Sloan Fellow. Dr. Rastetter is an R. B. Woodward Visiting Scholar of the Department of Chemistry and Chemical Biology at Harvard University. He is the author of numerous scientific papers and patent applications in the fields of organic and bio-organic chemistry, protein and enzyme engineering, and biotechnology. Dr. Rastetter holds a Ph.D. and an M.A. in Chemistry from Harvard University and an S.B. in Chemistry, Phi Beta Kappa and Phi Lambda Upsilon, from Massachusetts Institute of Technology.

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SAN DIEGO TECHNOLOGY HISTORY PROJECT

1 **INTERVIEWEE:** William Rastetter

2 **INTERVIEWER:** Matthew Shindell, Historian, UCSD

3 **DATE:** June 27, 2008

4 **SHINDELL:** It is June 27, 2008. This is an interview with William H. Rastetter. I am Mathew
5 Shindell. So, Dr. Rastetter, why don't you tell us, well, as far as you want to go back. At what
6 point did you become interested in biotech or things related to biotech? Was it during your
7 education or even prior to that?

8 **RASTETTER:** Well, I was an associate professor of chemistry at MIT and I think found work
9 within a very narrow defined discipline to be somewhat frustrating and confining, if you will.
10 And, saw the biotech industry starting with certainly some promise, (Shindell: Uhm-hmm.)
11 and I think the thing that struck me at the time was that it was an endeavor that was intensely
12 interdisciplinary and that, by its very nature, of interdisciplinary interaction, teaching,
13 learning, and collaboration was of interest to me. So I, I left the Department of Chemistry at
14 MIT and went to Genentech in the (Shindell: Uhm-hmm.) early days, and assembled a group
15 of actually very talented scientists who had gotten their PhDs, gone on and done postdocs, and
16 very good labs around the world. And, I think the thing that was unique about our group is
17 that we pulled together mathematicians, and x-ray crystallographers, protein chemists,
18 biochemists, microbiologists, molecular biologists, organic chemists, and had then collaborate
19 and create in an environment that I think at least at the time would have been impossible to
20 assemble within the academic sector.

21 **SHINDELL:** Uhm-hmm. And so at this point this is sort of the Boston biotech scene? And
22 how, how developed was that scene at that time?

23 **RASTETTER:** Well, that was Genentech. It was San Francisco.

24 **SHINDELL:** Oh, you, you had moved to San Francisco to do that?

25 **RASTETTER:** That's correct.

26 **SHINDELL:** Oh, okay. But, there is quite a large biotech sector in Boston?

27 **RASTETTER:** Certainly.

28 **SHINDELL:** So, were you exposed to that at all while you were at MIT?

29 **RASTETTER:** Well, most of the, most of the action was confined to about five companies at
30 the time, Cedes, Genentech, Amgen, Biogen. Biogen was in Cambridge and in Geneva,
31 Switzerland, but I had really no contact with (Shindell: Uhm-hmm.) Biogen at the time.

32 **SHINDELL:** And, how about before you were a professor at MIT? You got your degrees from
33 Harvard, is that right? You have an MS and a PhD in chemistry from Harvard?

34 **RASTETTER:** I have an MA and a PhD in chemistry from Harvard.

35 **SHINDELL:** Oh, an MA?

36 **RASTETTER:** Yeah.

37 **SHINDELL:** Okay. Was it not in chemistry?

38 **RASTETTER:** It was in chemistry.

39 **SHINDELL:** Oh, okay, but they don't, they didn't do an MS.

40 **RASTETTER:** Chemistry, chemistry is both an art and a science. [Laugh]

41 **SHINDELL:** Well, I think that's probably true, historically. (Rastetter: Right.) And in your
42 education had you thought at all about technology or biotech, or were you a more sort of
43 academic-focused student at that time?

44 **RASTETTER:** Well, I was doing chemistry at the interface with biology. Even as a graduate
45 student I was doing what became known as bioorganic chemistry, use of synthetic chemistry
46 directed at elucidating or mimicking biological mechanism or biological (Shindell: Uhm-
47 hmm.) molecules. And, it became pretty obvious to me that the tools of organic chemistry
48 were somewhat limited and one should use things like ribosomes, RNA, and so forth to make,
49 to make molecules. That is the tools that were evolving, (Shindell: Uhm-hmm.) coming out of
50 academia into these interdisciplinary groups at places like Genentech. So, I assembled one of
51 the first groups to do what has become known as protein engineering, (Shindell: Uhm-hmm.)
52 where you make mutants of naturally-occurring proteins as a very defined, very precise way
53 of studying structure and function, to understand how mutagenesis and changes of often
54 single amino acids change protein structure and function.

55 **SHINDELL:** Uhm-hmm. Okay. So you, you were doing work on the interface of chemistry and
56 biology pretty much throughout your entire career. So, how did your move into biotech
57 change your approach towards science, or towards innovation even? How would you
58 characterize the, the change in your own personal work?

59 **RASTETTER:** Well, I think the tools that are available to people who bring together many,
60 many disciplines' tools are, by definition, much broader. (Shindell: Uhm-hmm.) So, I can
61 think of engineering entire microbes, entire microbial pathways to make, to make new
62 chemicals. For example, (Shindell: Uhm-hmm.) we were able, in the early years, to take an
63 enzyme from corynebacter and put into our [winia][05:41] and eliminate the first seven steps

64 of the Reichstein Synthesis to make (Shindell: Uhm-hmm.) ascorbic acid by engineering a
65 microbe to do those steps. So it, it was the type of thing that would have been if not
66 impossible at the very least very difficult to do within a chemistry department.

67 **SHINDELL:** Oh.

68 **RASTETTER:** Right.

69 **SHINDELL:** And, is there anyone in particular who played a role in either convincing you to
70 make the transition to biotechnology or in facilitating that transition, or even a group of
71 people?

72 **RASTETTER:** Well, there was a fellow by the name of Ray Gomez who was on the faculty with
73 me at MIT who actually made the leap about a year before I did. (Shindell: Uhm-hmm.) And, I
74 stayed in touch with him and, you know, at the time it seemed like a brave new world, but he
75 convinced me that, you know, perhaps there was life after academia. [Laugh] He was
76 certainly correct. Uhm-hmm.

77 **SHINDELL:** Okay. And, so tell me how you wound up making the move from San Francisco
78 down to San Diego, if we're not missing anything in between there, if you want to talk a little
79 bit more about your (Rastetter: Yeah. Well I . . .) time in San Francisco.

80 **RASTETTER:** Sure. I was at Genentech for about five years and was recruited out of there by
81 someone at Kleiner Perkins Caufield & Byers, Byers in particular whom I had gotten to know.
82 KPCB was the founding . . .

83 **SHINDELL:** Was that Brook Byers?

84 **RASTETTER:** Yeah.

85 **SHINDELL:** Brook Byers?

86 **RASTETTER:** Yeah. KPCP was the founding venture capital firm behind Genentech. I'd
87 gotten to know Brook and he was starting a company in the antibody area and I agreed that,
88 that I would become the CEO. So. Easy as that. [Laugh]

89 **SHINDELL:** And, did you find it a different experience being the CEO of a company versus a
90 working scientist, or did you find you were able to maintain your role as a working scientist
91 even as CEO?

92 **RASTETTER:** Well, I'd say that the, the running of a group of twenty-five very talented
93 scientists at Genentech versus running a group starting even smaller than that at IDEC was
94 actually very similar. (Shindell: Uhm-hmm.) The problems were different, but the tools were
95 very similar. The pressures to perform, to stick to time lines, to raise capital and use capital
96 very efficiently were all the same. So no, I don't think it was very different at all. Ultimately,
97 at IDEC I was one of the inventors of Rituxan. It went on to become the world's, is today the
98 world's largest selling cancer drug. (Shindell: Uhm-hmm.) We'll have worldwide sales
99 somewhere between four and five billion, with a B, dollars this year. And so, I think often the
100 CEOs who are best prepared to make decisions that are good for small companies are CEOs
101 who have technical background, (Shindell: Uhm-hmm.) understand the risks inherent in
102 certain decisions, rather than relying entirely on the intuition of others who, who have the
103 training.

104 **SHINDELL:** Uhm-hmm. And could you elaborate on that a little bit, maybe with a story from
105 your own experience about how it is that your technical training helped you in that?

106 **RASTETTER:** Well, I will, again, give you the Rituxan example. IDEC was founded in 1986
107 around a similar technology involving use of antibodies to treat non Hodgkins B-Cell

108 Lymphoma. I say "similar" but at the same time it was extraordinarily different because the
109 technology that we started with was a customized approach to antibody therapy of
110 lymphoma. That is, if Mr. Smith would come in and be diagnosed with lymphoma we would
111 be able in three, four, maybe six months to make a monoclonal antibody for Mr. Smith. It
112 would work for Mr. Smith (Shindell: Uhm-hmm.) but it would not work, presumably, for
113 anybody else because it was customized only to his tumor. Recognize the, the very specific
114 antigen on the surface of his B-Cell tumor, an antigen known as an idiootype. We found by
115 about 1990 in our fourth year of existence that we had some absolutely remarkable
116 remissions of disease in lymphoma patients who had perhaps six, nine, twelve months to live,
117 (Shindell: Uhm-hmm.) and they would go into remissions of five, six, and seven years. The
118 unfortunate thing is that that would happen in only about twenty percent of the patients that
119 we treated. (Shindell: Uhm-hmm.) The other eighty percent treated with what would
120 become, if we commercialized it, a very expensive therapy, because it was customized to the
121 patient. The other eighty percent had responses that were really no better than what those
122 patients could achieve with fairly inexpensive chemotherapy, (Shindell: Uhm-hmm.)
123 relatively inexpensive chemotherapy. So, the pharmacoeconomics of the approach became
124 problematic to us. I mean, imagine a commercialized therapy that only works remarkably
125 well in twenty percent of the (Shindell: Uhm-hmm.) patients that has to be priced at like
126 \$50,000 per patient. The third-party payer wouldn't see that as a \$50,000 therapy. They'd
127 see it as a \$50,000 therapy that had worked in one patient in five (Shindell: Uhm-hmm.) so
128 they would see it as a \$250,000 therapy. (Shindell: Uhm-hmm.) So, I had to make the, at the
129 time, remarkably hard decision to abandon the technology around which IDEC had been
130 founded, and in 1993, two years after we had gone public and raised \$51 million to take this
131 customized therapy to the market I had to make the remarkably difficult decision to kill that
132 program (Shindell: Uhm-hmm.) and substitute a generic or off-the-shelf antibody, what's

133 known today as Rituxan in experimental clinical trials. And, you know, hindsight is pretty
134 good, you know. Today, I told you that drug will sell four to five billion dollars (Shindell:
135 Uhm-hmm.) worldwide, and so gosh that was a no-brainer. [Laugh] Right? Well no, we
136 didn't, we didn't know that at the time. (Shindell: Uhm-hmm.) And, the, the antibody was
137 designed, in fact, to, to eliminate not only the B-cell tumor but all the normal B-cells in the
138 patient's body. And so, there were two potential risks. One, would the patient survive the
139 massive tissue destruction of the tumor by this antibody? Would the kidneys, for example, be
140 able to withstand the, the influx of all these waste materials as the, the tumor would burst
141 open, as normal B-cells would be [liced][13:03] by the antibody. And number two, would the
142 patient survive without normal B-cells for long enough for the bone marrow to replenish the
143 normal B-cells? And, we didn't know the answer to either of those, (Shindell: Uhm-hmm.)
144 and I think there was some substantial risk in doing that. But, it seemed to me that the
145 alternative of taking both programs forward until we knew the answer to that was, was a
146 nonstarter because neither program would succeed because we, we wouldn't have the capital
147 to, (Shindell: Uhm-hmm.) wouldn't have the capital to get to answers with either one. I think,
148 in the end, we made the, the correct decision. I can remember sitting in a conference room in
149 Mountain View, California, where we had about half of our people at the time, and my
150 colleagues were arguing over a manufacturing issue with the customized therapy, (Shindell:
151 Uhm-hmm.) trying to figure out, "How can we make this more cost effectively?" and it, it just, I
152 kind of was daydreaming. I kind of went somewhere else, had kind of an out-of-body
153 experience, I suppose, and it dawned upon me [snaps fingers] that we, we needed to begin a
154 program with an antibody that could be made kilograms at a time, hundreds of kilograms at a
155 time, (Shindell: Uhm-hmm.) in large manufacturing vessels where you could make the stuff
156 really very inexpensively. And so, with the combination of, of business training and scientific
157 training was able to understand the inherent risks and unilaterally made the decision to go

158 with a new program and eliminate the, the old one. I guess that's the, the luxury of being and
159 the risk of being a CEO. (Shindell: Uhm-hmm.) Fortunately, I was right. So.

160 **SHINDELL:** And, did you get much resistance to that decision?

161 **RASTETTER:** Oh, absolutely. (Shindell: Yeah.) Most of the founders left, (Shindell: Uhm-
162 hmm.) left the company.

163 **SHINDELL:** Well. Let's step back a second to the more general picture for a second, because I
164 realize we didn't really touch on this. What about sort of the academic science versus the
165 culture of, of biotechnology, and sort of corporate science and innovation? (Rastetter: Uhm-
166 hmm.) Did you notice a big difference between those two cultures and how did you deal with
167 that? And then, sort of related to that, how did your academic colleagues treat you once
168 you've made this move into corporate science?

169 **RASTETTER:** Uhm-hmm. [Train noise in background] [_____] [15:39].

170 **SHINDELL:** Okay. Sure. [Conversation in background][Recording paused][15:58] Well,
171 maybe I just need to – there we go. Now we're started again. Okay. So, back to that question,
172 the cultures of academic science versus corporate science and the ways in which maybe the
173 new culture, the ways in which you took to the new culture or adapted to the new culture, and
174 then also how your academic colleagues treated you once you'd made that move?

175 **RASTETTER:** Uhm-hmm. Well, I think the cultures are, are remarkably different and perhaps
176 not apparently so to someone who's been immersed in the academic sector for a long time.
177 (Shindell: Uhm-hmm.) I think generally in the academic sector we think of the superstars as
178 being individuals. (Shindell: Uhm-hmm.) In the corporate sector, at least among companies
179 that I think are good companies, productive companies, superstars are teams. And, often
180 there is no place within the corporate culture for the, let me call it the "prima donna"

181 superstar (Shindell: Uhm-hmm.) that might thrive in the academic sector. And, I like to think
182 of the distinction in the corporate sector. I mean don't, don't get me wrong. You want very,
183 very good people in, in the, in the industrial sector, but I think the distinction, the very
184 important distinction is that between the prima donna and the leader. (Shindell: Uhm-hmm.)
185 Okay? The prima donna is very "me, me, me, me, me" focused and "Look at the papers I've
186 published. Look at the ideas I've generated. Look how many seminars I'm invited to give.
187 Look how many awards I've gotten," etcetera, etcetera. And that's, that's fine within that
188 culture. In fact, those who succeed do all of those things, (Shindell: Uhm-hmm.) and do them
189 in spades. The, the "me, me, me" person doesn't do nearly as well in the industrial sector,
190 because the "me, me, me" person isn't a very effective leader. (Shindell: Uhm-hmm.) Okay? A
191 leader has to be able to motivate, to coalesce, to communicate, to cause a group of people to
192 become much more than the sum of its parts. And so, the intense focus has to be on the
193 individuals that, the focus of the leader must be on the individuals who form the team, has to
194 be on the job at hand, has to be on the deliverables, the timelines, and so forth, but also has to
195 be focused on providing for the team members context, big picture. (Shindell: Uhm-hmm.)
196 That is, the teams who maybe well coordinated and communicate well, but where every
197 individual only knows their little piece and knows when to hand off aren't nearly as effective
198 as teams that really understand the context of what they're doing, why it's important, how it's
199 differentiated, why it's going to make a difference in peoples' lives. (Shindell: Uhm-hmm.) So,
200 the "me, me, me" guy from the academic sector isn't often very effective industrially, because
201 he or she doesn't understand the nuances (Shindell: Uhm-hmm.) of leadership and team
202 coalescence. Does that, that make any sense?

203 **SHINDELL:** Yeah. Yeah.

204 **RASTETTER:** Okay.

205 **SHINDELL:** Where do you think you learned those skills? Did you know them prior to
206 entering the industrial sector or is this something you had to learn on the job once you made
207 that move?

208 **RASTETTER:** You know, I probably didn't expect that there would be any cultural difference
209 between academia and, and industry, and so I think that came as a bit of, you know, cold
210 bucket of water in the face. (Shindell: Uhm-hmm.) Because, I was kind of used to being the
211 focus of attention, whether I was, you know, teaching six hundred premeds, or leading a
212 research group kind of one-on-one with individuals. (Shindell: Uhm-hmm.) And, all of a
213 sudden you had to learn about teamwork and making these twenty-five people produce what
214 fifty individuals working alone couldn't possibly do. Right? (Shindell: Uhm-hmm.) So. But,
215 you know, I think, I think I, with some help and coaching from the right people was able to
216 pick that up.

217 **SHINDELL:** Is there anyone in particular that you think, in terms of coaching, anyone in
218 particular who had an influence on your management style?

219 **RASTETTER:** No. I don't think any single individual stands out. I think it is a mix of good
220 examples and bad examples. [Laugh] I think it's important to learn from both, from both
221 sides. Yeah.

222 **SHINDELL:** And, I'm sure learning from mistakes as well is instructive? Do you remember
223 any sort of anecdotes from your early days in this that would sort of demonstrate the
224 confrontation of maybe the old you with the new environment? Or . . .

225 **RASTETTER:** Oh, none that come to mind immediately. But . . .

226 **SHINDELL:** No? [Laugh] Well, that's okay. We can move forward. And, if any occur to you
227 while, while you're talking (Rastetter: Okay.) please, you know, go ahead and, and tell them.

228 Now, what about your academic colleagues? Did they view you with suspicion once you
229 moved out of academia or did you find your relationships with them stayed pretty much the
230 same?

231 **RASTETTER:** Well, I think the move to Genentech from MIT was seen as, as a fairly daring
232 move. (Shindell: Uhm-hmm.) Genentech certainly had a reputation for attracting some of the
233 best academic minds in the world. And so, it wasn't, it wasn't as if I was leaving a center of
234 academic excellence to go to ABC Commodity Chemical Corp or, (Shindell: Uhm-hmm.) you
235 know, just to make up a disparaging word, disparaging name. So, certainly the types of
236 problems that Genentech was, was tackling at the time had never been solved before, were
237 directed at good purposes, development of human therapeutics and so forth. Human
238 therapeutics that were quite different from what had, you know, come out of small molecule
239 work. So, I think there was perhaps some, "Wow, he's, he's nuts to, to do this," (Shindell:
240 Uhm-hmm.) among some, and perhaps others were, "Wow, you know, if anybody's going to
241 succeed Genentech will succeed. This is a good, good move. (Shindell: Uhm-hmm.) This
242 should be a good adventure." I think, though, most people reserved judgment. I think, in the
243 end, there was, there, there is today, if I may say so, some admiration for what I did with the
244 discovery, development, and commercialization of the first monoclonal antibody approved by
245 the FDA for cancer therapy (Shindell: Uhm-hmm.) that has become the largest selling cancer
246 drug in the world. So, I think at least with, with hindsight my colleagues today tend to greet
247 me quite warmly and without, without disdain. [Laugh]

248 **SHINDELL:** Uhm-hmm. These days it seems like there are a lot of people who manage to
249 maintain their academic posts while also working in, in biotech. Maybe not on the level that
250 you were working. Was that possible at the time or was it, is that a more recent phenomenon,
251 that people are able to stay at UCSD, for example, while also being on the board of one or two
252 biotech companies?

253 **RASTETTER:** Well, I think it's quite different being on the Board (Shindell: Uhm-hmm.) and
254 being engaged in real day-to-day decision making. I serve on the Board of a local company, a
255 very successful local company, Illumina, where the founder, David Walt from Tufts University,
256 is still on the Board and contributes a tremendous amount, but is employed full-time by Tufts
257 as a professor in the Chemistry Department. (Shindell: Uhm-hmm.) The, you know, the
258 involvement of Board members is more for governance, strategy, and oversight. It's quite
259 different from the day-to-day activities of the company. (Shindell: Uhm-hmm.) So, I think
260 scientists who believe they will split their time for day-to-day work between academia and
261 the industrial sector will probably do neither job as well as if they committed to one or the
262 other.

263 **SHINDELL:** Oh really? Okay. Well, let me ask you then, while we're on this subject, about sort
264 of more generally, what do you think the role is of the university and of university scientists in
265 a successful biotech sector? And, in answering this, I mean, you could, you could talk about
266 the specific San Diego example and how UCSD, and Scripps, and the other institutions maybe
267 play a role in the success of the sector here? Although that one (Rastetter: Sure.) success
268 shouldn't, you know, color your answer if you feel like it's not a healthy relationship or it's not
269 as good as it could be.

270 **RASTETTER:** Well, I'm, I'm going to step way back in answering the question and I'm going
271 to go to the national level first. (Shindell: Okay.) And, I think it's quite clear that United States
272 is pre, preeminent in biotech. There are other regions who are doing it, but certainly we led
273 and maintain, by far, the critical mass of people, of discovery, of successes in terms of product
274 launches, in terms of innovation. And, I think the uniqueness of biotech in the U.S. comes from
275 a three-legged stool, if you will. (Shindell: Uhm-hmm.) One is the National Institutes of
276 Health and the often-enlightened funding that Congress has provided. (Shindell: Uhm-hmm.)
277 Though, certainly I think that's jeopardized today. There is a common misperception among

278 the U.S. public that the National Institutes of Health has developed all these wonderful drugs
279 that we enjoy and pharmaceutical industries are just kind of marketing arms. (Shindell: Uhm-
280 hmm.) That's certainly not the case. The NIH has, perhaps, taken one or two drugs, in their
281 entire existence, all the way through to (Shindell: Uhm-hmm.) approval and
282 commercialization, or out-licensing. But the, the extraordinarily important thing that the NIH
283 has done is to provide the capital and the ability to educate and inform individuals with
284 interest in biological and life sciences on, in the tools, the theories, the methods of science that
285 are applied to biotech problems. And, without that funding the science that we call
286 biomedicine, if you will, would be confined to the pharmaceutical companies. (Shindell: Uhm-
287 hmm.) And, the richness of discovery, even within the pharmaceutical companies, would be
288 curtailed. I think it is the, the funding of academic research through the NIH, the extramural
289 grants and whatnot, that has ceded the ideas, the intellectual property, has given incentive to
290 the people who have become the founding scientists in, in biotechnology. So, that's one leg of
291 the three-legged stool. (Shindell: Uhm-hmm.) The second leg is venture capital. And clearly,
292 in primarily the Bay Area and the Boston area venture capital firms are very plentiful. There's
293 a lot of capital that can be deployed for really, really good ideas, or really, really good people
294 have good IP protection and want to start companies. And, I think that while there is some of
295 that in Europe, it doesn't parallel what we have in, in the U.S. (Shindell: Uhm-hmm.) The
296 third leg of the stool is the NASDAQ, and the ability to take companies that have parlayed
297 forty, fifty, maybe sixty, or seventy million dollars from venture and partnering sources into
298 public companies that have access to public capital. And, the three of those together have
299 been, have been remarkable for, for creation of biotech industry. Now, how does that apply to
300 San Diego? Well, with Scripps, Clinic and Research Foundation, with the Burnham, with the
301 Salk, with UCSD, with what, I'm guess, twenty-five, thirty thousand people employed in this
302 area (Shindell: Uhm-hmm.) in, in the biosciences, and a lot of that funded by NIH funding, we

303 have a very rich, very rich environment for the starting of companies. (Shindell: Uhm-hmm.)
304 Okay? And, venture capital is available. There aren't as many venture capital firms down here
305 as they are in the Bay Area but, you know, it's, what, an hour and a half flight away. So, and
306 certainly the NASDAQ is available to us. I think some of the difficult decisions that local
307 organizations have had to make relate to access to capital. For example, Scripps has had a
308 number of relationships with large pharmaceutical companies (Shindell: Uhm-hmm.) where
309 they have sort of an exclusive relationship with, with one pharmaceutical company at a time
310 that lasts for a number of years, and I think that has constrained the flow of intellectual
311 property out of the Scripps, because the large pharma partner has had really first right to
312 negotiate these things. (Shindell: Uhm-hmm.) And only when they pass can these things
313 become companies. So, while that access to capital, I think, and large amounts of capital has
314 been very good for the organization per se, I don't think it has spawned as many companies as
315 might have been spawned had there been equal funding with less restrictions applied to them.
316 (Shindell: Uhm-hmm.) Yeah.

317 **SHINDELL:** And, do you feel that the closeness of the companies and the universities here in
318 San Diego plays a role? And, by that I mean is there a geographical closeness, the fact that the
319 cluster sort of literally is geographically a cluster and people see each other quite a bit due to
320 that fact? Do you think that plays a role in the process of innovation here or the success of
321 companies here?

322 **RASTETTER:** Well, I think it makes access to human capital much easier. (Shindell: Uhm-
323 hmm.) I think it makes interaction to borrow equipment or to share space for an animal
324 facility, or something like that you know, much easier. I guess the other side of that is that
325 companies tend to conduct their research for reasons of intellectual property protection
326 under kind of a shroud of secrecy. (Shindell: Uhm-hmm.) So there, it isn't as if twenty local
327 biotech companies are like twenty small universities (Shindell: Uhm-hmm.) that are sharing

328 ideas with each other. It just doesn't work that way. But, I think one of the, one of the things
329 that we really benefit from down here is that most of our biotech companies reside within the
330 same city, City of San Diego. (Shindell: Uhm-hmm.) And so, there's a single set of regulations
331 and fairly easy to get the attention of the right people in the city and get your permits, and so
332 forth. In the Bay Area, the companies up there are spread among, I mean jeeppers, you know,
333 there's Redwood City, and there's Palo Alto, and there's Menlo Park, and there's Atherton, and
334 there's South San Francisco, and Burlingame, and San Mateo, and – I mean, whoa. Who are
335 you dealing with? Well, you're dealing with a number of municipalities, (Shindell: Uhm-
336 hmm.) but none of them really has the critical mass that we have here in terms of having one
337 central place in the city. So, I think that has made it easier here. The commute, at least to-
338 date, is a bit easier down here because we don't have bridges, and bays, and (Shindell: Uhm-
339 hmm.) whatnot. (Shindell: Uhm-hmm.) Interacting with people in the East Bay, in the Bay
340 Area, if you are on the Peninsula, is a hassle. You can pick up the phone. You can email them.
341 But, actually getting over to a seminar in the East Bay is something you probably would do
342 with some trepidation. Much easier here (Shindell: Uhm-hmm.) if you're in a biotech
343 company to go over to Scripps to watch a seminar or something. So yeah, I think the cluster is
344 important. The cluster has changed in its character. I've been in San Diego now for twenty,
345 twenty-one going on twenty-two years and I think that twenty-two years ago the cluster here,
346 with some exceptions, were, the cluster was populated by a bunch of refugees from academia.
347 That is, mainly people who were still trying to figure out how to do this thing called
348 "biotechnology." (Shindell: Uhm-hmm.) Now it's a much more mature cluster where you
349 don't really have to go outside of the San Diego area to recruit, and you can get just about
350 anybody you want, from manufacturing, to quality, to regulatory affairs, to clinical science. In
351 other words, the things that you don't normally practice in a biology department or chemistry
352 department, but are absolutely necessary within biotech, are now here. (Shindell: Uhm-

353 hmm.) That is, the professional staff that are required to build a fully-integrated company are
354 now available, (Shindell: Uhm-hmm.) and they were no twenty years ago.

355 **SHINDELL:** I remember, I read one paper that characterized that early stage of development
356 of, of the biotech sector here as, you know, the high-risk time period of getting involved in
357 biotech, and that maybe (Rastetter: Uhm-hmm.) those sort of initial companies laid down a
358 sort of a backbone that has made it far less risky, although still risky, to start companies today.
359 Would you agree with that assessment and if so, what are the major steps do you think that
360 happened to, to lay down that backbone?

361 **RASTETTER:** Well, one of the most important pieces was the acquisition of Hybritech by
362 Lilly. (Shindell: Uhm-hmm.) And, what we saw at the time were the, the doors at Hybritech
363 flew open and everybody just escaped, went out and started companies. (Shindell: Uhm-
364 hmm.) Right? So, that was, that was good for seeding of little pockets of talent, and ideas, and
365 intellectual property that became a number of companies. Right? (Shindell: Uhm-hmm.)
366 Gensia, and Genta, and Gen-Probe and, you know, the list goes on. It was, it was a risky time.
367 It is certainly not risk-free today. I think the risks have changed. I . . . the uniqueness of the
368 biotech sector in 1986, to pick a year, was that large pharma didn't have many of those skills.
369 (Shindell: Uhm-hmm.) Okay? Biotech, today, is riskier because large pharma does have those
370 skills, (Shindell: Uhm-hmm.) either through acquisition or through, in some cases, organic
371 growth of, of groups that have, you know, protein biologics-based people in science. The, the
372 risks back then were also, to some extent, lower because some of the targets were obvious.
373 Let's make real human insulin rather than bovine or porcine insulin. (Shindell: Uhm-hmm.) I
374 mean, you knew it was going to be effective. (Shindell: Uhm-hmm.) There was very little
375 clinical risk. It was, "How do we make this? How do we formulate it?" Well, even the
376 formulation, you know, is pretty, pretty much a cinch from the formulation of the very similar
377 porcine or bovine material. Or, "Let's make growth hormone. Rather than from cadavers let's

378 make it in e coli." And so, a lot of those risks, a lot of those targets with reduced risk, don't
379 exist today. (Shindell: Uhm-hmm.) Okay?

380 **SHINDELL:** So, the obvious ground has been covered, basically?

381 **RASTETTER:** A lot of it has. Yeah. (Shindell: Yeah.) Yeah. The biology that we're dealing
382 with today, I think, is much more complex. I think we're talking about SNP genotyping, we're
383 talking about whole genome sequencing and trying to pick patients for certain therapies, or
384 avoiding certain therapies in certain patients. (Shindell: Uhm-hmm.) And, you know, just the
385 bioinformatics has gotten tremendously complex. We're talking about systems biology where
386 entire metabolic systems are the target rather than single receptors or enzyme active sites.
387 We're talking about tissue regeneration in stem cells, good or bad. Stem cells for tissue
388 regeneration or stem cells that cause cancer. (Shindell: Uhm-hmm.) So these are, the
389 problems get more and more complex and more and more difficult. So, still, it's still risky.

390 **SHINDELL:** Yeah. Let me ask you about organizations that have also played a role. What
391 about organizations such as, for example, UCSD CONNECT, and also maybe in a different sort
392 of capacity, Biocom, and the roles that they have played here in solidifying the biotech sector
393 or, you know, helping to make it stronger or more successful?

394 **RASTETTER:** Uhm-hmm. Well, I think organizations like Biocom and CONNECT have been
395 particularly important for the entrepreneur who doesn't have all the connections, all the
396 relationships within the community. The ability, for example, for a small company to use and
397 leverage the purchasing power of forty or fifty companies for the Biocom Purchasing Group.
398 You know, obviously, if you're negotiating for fifty companies you have a lot more leverage
399 with the vendors than (Shindell: Uhm-hmm.) if you're a small company just getting started.
400 So, yeah, no. I think these things have been very important. They, they're kind of the glue that
401 holds the cluster together.

402 **SHINDELL:** Uhm-hmm. A couple of people who I've interviewed, for example Howard
403 Birndorf and Bill Comer, (Rastetter: Uhm-hmm.) they both pointed to Bill Otterson (Rastetter:
404 Uhm-hmm.) as being instrumental in sort of creating the atmosphere of San Diego biotech, of
405 sort of collaboration among companies, and making people come together on a, on a frequent
406 basis. Was that your experience (Rastetter: Uhm-hmm.) as well?

407 **RASTETTER:** Yeah. Absolutely. Bill was an intensely social, collegial, collaborative, cohesive
408 force in the community. (Shindell: Uhm-hmm.) Absolutely.

409 **SHINDELL:** Okay. Let me ask you something a little bit more maybe nuts and bolts about
410 your experience with biotech. Prior to going into biotech I'm guessing you didn't have any
411 experience with the patenting process and how that might affect the research process. Could
412 you say a little bit about how patents – or first, you know, whether patents were an obstacle to
413 you at first, or whether you feel like these things are important for the research process in
414 biotech? You know, basically, what's your view on, on the patenting process?

415 **RASTETTER:** Well, patents are absolutely critical for biotech as it relates, let's say, to
416 therapeutic product development. It took us, from company founding to the FDA approval of
417 Rituxan took us eleven years. (Shindell: Uhm-hmm.) Now, if somebody could come along and
418 rip off, if you will, that invention, those eleven years from us, the next day, there would have
419 been no incentive to invest that capital. (Shindell: Uhm-hmm.) So, we would not have had
420 capital to develop the product. I guess what I'm trying to say is that the longer the
421 development cycle – eleven years is pretty fast, actually, (Shindell: Uhm-hmm.) from concept
422 to, from founding actually. From concept it was seven years, which is perhaps a record for
423 something of that magnitude. But, the longer the development cycle the more important
424 patents become. If you can show what compositions matter, how to use them, what clinical
425 setting, what doses, how to formulate, how often to treat, easy for somebody to come, come

426 along and copy it. (Shindell: Uhm-hmm.) Okay? On the other hand, at the other end of the
427 spectrum, devices that can be produced and marketed without regulatory approval, say, not
428 necessarily for human healthcare, maybe, you know, a new mouse or a new flat screen or
429 whatever, it can be (Shindell: Uhm-hmm.) developed in twelve or eighteen months, I think
430 patent protection is less important because there's more than one way to skin a cat (Shindell:
431 Uhm-hmm.) for those and the development cycle's much shorter. So, it isn't always obvious
432 that someone needs to infringe your patent on your mouse in order to make a better mouse.
433 (Shindell: Uhm-hmm.) But, you know, because of patent protection, Rituxan's been on the
434 market for over ten years and nobody has come along and ripped it off. So, the incentive still
435 exists for (Shindell: Uhm-hmm.) people to invest for a decade to a decade and a half to get
436 (Shindell: Uhm-hmm.) these medicines on the market. Patents are absolutely critical.

437 **SHINDELL:** Uhm-hmm. Do you think that they've at all changed the way that academic
438 scientific research is done now that there's sort of this model of university scientists patenting
439 their discoveries, founding companies? Do you think that university scientists think of their
440 work in a different way now that there is the potential that they could, say, at, they're working
441 at UCSD, they're so close to this cluster, if they have a discovery they can patent it and make
442 money as well? Do you think this changes the way that they do their work or how they think
443 about their work?

444 **RASTETTER:** Well, probably that question would be best answered by a group of academic
445 scientists, (Shindell: Uhm-hmm.) and I think what you would find is that the answer is fairly
446 personal and fairly individualized, (Shindell: Yeah.) and is probably, varies also by scientific
447 field. (Shindell: Uhm-hmm.) Right? People developing nanoparticles within a Department of
448 Materials Science are probably acutely aware of the importance of patents as it relates to
449 being able to deploy their science, their technology, into the commercial sector. At the other
450 extreme, a mathematician, who's developing a new proof of a theorem or something probably,

451 you know, has no, no reason to even think about patents. (Shindell: Uhm-hmm.) Right? And
452 so, I think it's, I think it's field-specific, but I think it's also depends on, on the individual.
453 (Shindell: Uhm-hmm.) Some individuals may dream about starting a new company and
454 participating, at least from their academic perch, and the thrill and the victory of taking a
455 company public and getting products launched, and whatnot. I think those people will be
456 more aware of the importance of patents (Shindell: Uhm-hmm.) than folks who may not be so
457 keenly interested in the, you know, if they're more theoretically inclined. (Shindell: Uhm-
458 hmm.) The theoretical physical chemist, for example, at least in certain fields, may not be as
459 interested in doing that as (Shindell: Uhm-hmm.) compared to a biologist studying the
460 immune system and how it can go wrong in autoimmune disease. (Shindell: Uhm-hmm.)
461 Right?

462 **SHINDELL:** Yeah. Well, let me rephrase the question a little bit so you can speak maybe more
463 from your, your own personal experience. Do you have university scientists come to you on
464 any sort of regular basis, maybe, saying, "Bill, do you think this is patentable or do you think
465 that I should follow this line of research?" I mean, do they look to people like you, with
466 expertise in patenting or expertise in the biotech sector, with questions about their research
467 and whether or not it's marketable?

468 **RASTETTER:** Well, I'm currently a partner in Venrock, which is one of the large venture
469 capital firms, and so on a weekly basis I interact with academic scientists, or scientists who
470 have licensed or proposed to license things out of academia. I would say that it isn't often the
471 question, "Should I patent this?" It is often, "Look, patents have been filed, or patents have
472 been issued, this is my intellectual property (Shindell: Uhm-hmm.) fortress and this is why
473 you should give us some capital." So.

474 **SHINDELL:** So, they mark their territory first before coming to you, most of the time?

475 **RASTETTER:** Well, sure. (Shindell: Yeah.) If they're coming looking for venture capital
476 they'd better have their (Shindell: Uhm-hmm.) IP ducks in a row or we probably wouldn't talk
477 to them. [Laughter] Right. No, I think, I think people seeking to, to found companies and to
478 get capital are reasonably sophisticated in these things, (Shindell: Uhm-hmm.) and we will
479 always do a, an intellectual property due diligence through an outside patent lawyer or patent
480 law firm before we invest. (Shindell: Uhm-hmm.) It's a critical step.

481 **SHINDELL:** Oh, okay. Now, back to the question of San Diego and Biotech Beach. How would
482 you compare San Diego's biotech sector to say, you know, Boston's, and San Francisco's?
483 Aside from the fact that things are closer together, do you feel like – well, how do you feel like
484 this sector compares to those other two?

485 **RASTETTER:** Well, the other, the other two have a little more history under their belts, so the
486 successful companies have, are older, and have gotten somewhat larger. I think that we see,
487 however, the growth of successful cash-flow-positive companies. I mean, after all that is the
488 objective, isn't it, to become profitable and (Shindell: Uhm-hmm.) self-sustaining so you don't
489 have to always rely on NASDAQ and venture capital. But we, we see an increasing number of
490 companies, who have made that jump, IDEC, now Biogen Idec, Illumina, Invitrogen, Amylin.
491 (Shindell: Uhm-hmm.) So, I think we are maturing as a sector in San Diego, and the two most
492 important hallmarks of that are more large companies, cash-flow positive profitable
493 companies, and a greater diversity of the professions from soup to nuts that are required to
494 run a fully-integrated company (Shindell: Uhm-hmm.) within the cluster. Okay?

495 **SHINDELL:** It seems like for a long time San Diego was very strong in sort of maybe the
496 discovery side of biotech, but development was maybe stronger in these other sectors. And,
497 do you think that development is maturing here? Is that, is that what is one of the hallmarks
498 of a mature biotech sector and do you see that happening here?

499 **RASTETTER:** Yeah. Well, the conventional wisdom is that what biotech companies do is
500 discovery, development, manufacturing, clinical trials, and commercialization. And, I think
501 that often is a recipe for failure. (Shindell: Uhm-hmm.) I think that successful companies
502 have to start with development, manufacturing, clinical trials, commercialization, and then go
503 back to discovery. (Shindell: Uhm-hmm.) That is, they need to find something that is mature
504 enough where a lot of the science and biology risk has been removed from it so that they don't
505 spend all of their capital doing discovery only to find that they don't have enough to show for
506 it in terms of progress into the clinic to raise enough capital to actually get there. (Shindell:
507 Uhm-hmm.) And so, I think one of the mistakes that a lot of biotech companies have made, not
508 only in San Diego but elsewhere, is to think that if they focus on discovery and just do that
509 well enough that people will come running to their door with more capital to take these things
510 forward. Well, they ignore the fact that as you move down this pipeline from discovery, to
511 development, to manufacturing, to clinical, to commercialization you're using more, and more,
512 and more, and more money per unit of time. (Shindell: Uhm-hmm.) And, simply defining a
513 molecular entity through discovery that you want to take forward doesn't reduce the risk
514 sufficiently (Shindell: Uhm-hmm.) to get the investor to be so enticed that they're going to put
515 this huge amount of capital into taking it forward. So, I think the staging, that is the point at
516 which you decide you're going to raise capital and bring people together, is very, very
517 important and I think it has to be around something that's fairly well understood so you don't
518 have to spend, you know, twenty, thirty, forty million dollars to do discovery. (Shindell: Uhm-
519 hmm.) So, yeah, I think that is being learned but I think it's being learned the hard way. Right.
520 When we founded, when we founded IDEC the customized antibody therapy was already in
521 the clinic. We already knew how to manufacture it, not cost-effectively but knew how to
522 (Shindell: Uhm-hmm.) manufacture it. And, the things that we learned about formulating,
523 about quality control, about the stability of antibodies, how to keep them in acceptable form

524 for human delivery, the things that we learned about how antibodies are distributed within
525 the body, how fast it takes them to get into lymphatic systems, all that stuff, all that know-how
526 was directly transferable to Rituxan when we had Rituxan. So, and all of it was very
527 development oriented but all, all that know-how, all that knowledge, all those skills were
528 directly transferable to the new product. (Shindell: Uhm-hmm.) So, very important.

529 **SHINDELL:** And, was much of that sort of developed at Hybritech prior to IDEC? Because,
530 they were sort of the first to work with monoclonals?

531 **RASTETTER:** Yes, but you have to realize that Hybritech was focused on in vitro diagnostics,
532 (Shindell: Uhm-hmm.) where they're using tiny amounts of monoclonal antibodies. We
533 needed to make grams at a time. When we started IDEC we knew we would have to deliver
534 maybe three or four grams of antibodies (Shindell: Uhm-hmm.) to patients for a full-course of
535 therapy. And, in 1997, I'm sorry, 1987 I called my friend Charlie Benton, who ran Antibody
536 Manufacturing Company in St. Louis, and I said, "Charlie, we've got to decide whether we're
537 going to become experts at manufacturing or whether we're going to outsource
538 manufacturing, and so I'd like for you to think about this question. I'm not going to negotiate
539 with you. I'm going to ask you, as a preferred customer how much would it cost if we didn't
540 manufacture, if we did it all with you, how much would it cost per gram of antibody
541 manufactured?" And, gave him some parameters about the hybridomas that we were using,
542 and whatnot, and I said, "Just get back to me with a single figure. With that figure I can go to
543 my colleagues and we'll make this very important decision for the company." And, he got back
544 to me and, this is 1987 so 1987 dollars, and he said, "Bill, we would love to have your business
545 and we think we can deliver to you, as bulk product, monoclonal antibodies for \$5,000 a
546 gram." (Shindell: Uhm-hmm.) Okay? I said, "Charlie, thank you. Goodbye. We're going to
547 make them ourselves." [Laugh] Well, today Rituxan is made for – I don't want to give away
548 any proprietary information – [Laugh] but let's say somewhere in the \$100-\$200 gram range,

549 (Shindell: Uhm-hmm.) and you give, you give about four grams to a patient a year. Well gosh,
550 you know, at Charlie's price the selling price is, I mean, what you'd get for bulk product. So, it
551 would have been impossible (Shindell: Uhm-hmm.) with the technology back then. (Shindell:
552 Uhm-hmm.) So the, the elements of process development, of how you do these things, on a
553 scale that enables therapeutics is not something that Hybritech had developed, because they
554 weren't using – I mean, grams of antibodies would be enough for ten thousand patients, right
555 (Shindell: Uhm-hmm. Uhm-hmm.) for in vitro diagnostics.

556 **SHINDELL:** Well, that's interesting. According to Birndorf, they were sort of convinced by
557 their investors, when they started Hybritech, Brook Byers and others, that they should
558 actually focus on therapeutics as well, but I guess they never got to that stage at Hybritech?

559 **RASTETTER:** You know, they, they tried for awhile. I think it is extraordinarily difficult for a
560 small company to have a business and cash flow and profitability that depends on one use of a
561 technology (Shindell: Uhm-hmm.) to actually create and nurture a separate group that uses
562 the same technology for a completely different purpose, where the cost of goods, where the
563 delivery, the purity, everything else has to be extraordinarily different. (Shindell: Uhm-hmm.)
564 And, now, did the acquisition of Hybritech by Lilly help Lilly understand the development of
565 biologics? Don't know. You have to remember that Lilly took the Genentech process for
566 human insulin (Shindell: Uhm-hmm.) and adapted it to full-scale fermentation and
567 commercialized the human insulin way long before they, they bought, they bought Hybritech.
568 So, I don't know. (Shindell: Uhm-hmm.) But, and certainly there was some knowledge about
569 quality and formulation and so forth for human use that Lilly got from that. But, I think
570 Hybritech will be remembered for their contributions to in vitro diagnostics. Certainly not for
571 antibody therapeutics.

572 **SHINDELL:** Uhm-hmm. Let's see. I think you've addressed much of these sections. So, since
573 we're coming up on an hour maybe we should go to the last part of the interview then. So
574 these, these are questions that relate most specifically to your, your own career and your own
575 experience. So, what do you think, based on your own experience, was the most important
576 change in Biotech Beach during your time here? Do you think there was any one thing that
577 stands out, or it may be even more than one thing that stands out as, you know, a pivotal
578 moment in your time here?

579 **RASTETTER:** Well, the pivotal moment for me personally, professionally, and for the
580 company was the approval of Rituxan the day before Thanksgiving 1997. [Laugh]

581 **SHINDELL:** Must have been a good Thanksgiving?

582 **RASTETTER:** Yeah. It was a darn good Thanksgiving. You know, cash flow, self-sufficiency,
583 the ability to fuel your company through product, product sales is the objective of every
584 company. I, [Laugh] I went to, I went to Havana, Cuba to teach a week of business school.
585 (Shindell: Uhm-hmm.) I was part of a group from the Rockefeller Foundation and had been
586 invited to go down and teach the tools of capitalism to the 1,500 people in Cuba who do
587 biotechnology. And, I was asked to spearhead a group that looked at all their efforts in
588 biotech, in Cuba, and what I saw was about 1,500 people doing human therapeutics, human
589 diagnostics, or doing vaccines. They were doing transgenic animals. They were doing
590 industrial chemicals by microbial pathway engineering. They were doing industrial enzymes.
591 I guess thinking about commodity chemical production, and so forth. And, they asked the
592 group to critique it, and I was the spokesperson. At the time they had commercialized, in
593 countries where there was no patent protection, streptokinase for blood clots. They had alpha
594 interferon for a variety of uses, and had hepatitis-B vaccine. (Shindell: Uhm-hmm.) So, they
595 know how to develop stuff, okay? And, they were doing all this discovery research all over the

596 place and when asked to critique it I said, "Well, look, it seems to me, based on the cash flow,
597 that you generate from streptokinase, alpha interferon, and hepatitis-B vaccine that you can
598 probably take four hundred of these 1,500 people that are doing biotechnology and call them
599 "company" and take 1,100 and call them "university," (Shindell: Uhm-hmm.) and have the
600 university do the discovery stuff (Shindell: Uhm-hmm.) and have the four hundred do the
601 stuff that's very development oriented, that is closest to human application and/or
602 commercialization, as the case might be. And, in order to do that you've got to pick one field
603 because four hundred people can't possibly be good at doing all these things that you're doing.
604 (Shindell: Uhm-hmm.) And so, pick something. And, it seems to me it's probably human
605 therapeutics, if you look at alpha interferon, and streptokinase, and hepatitis-B vaccine.
606 Vaccine is not quite therapeutics, but I think that's what you should do." And, I drew this
607 picture up on the blackboard where I had a dollar sign and then over the arrow the word
608 "stock" implying the sale of equity in the company to fuel R&D. And then from R&D I had an
609 arrow that came down. I'm going to form a full circle here. R&D to products to sales,
610 generating dollars, closing the loop to R&D, and then I put a big X through the stock sales.
611 (Shindell: Uhm-hmm.) And my point was that "If you succeed after you've seeded the
612 company with selling some initial stock to venture capitalists, through the NASDAQ, whatever,
613 the objective of any company has to be to become self-sustaining. (Shindell: Uhm-hmm.) In
614 order to do that you have to know what you do, what you can become the best in the world at.
615 (Shindell: Uhm-hmm.) And so, you guys need to focus and you need to separate this
616 academia from corporate, and the corporate has to be incredibly focused on doing one thing
617 and doing it better than anybody else in the world (Shindell: Uhm-hmm.) if you really want to
618 succeed and have that circle get bigger, and bigger, and bigger, and bigger, because you have
619 more and more products and more and more sales, hence more and more R&D (Shindell:
620 Uhm-hmm.) and generate this, this perpetual loop, this cash flow machine." Well, I finished

621 my speech, my analysis, my recommendation, and there was this room, it was probably 150 of
622 the managers of the 1,500 people who do biotech in Havana, Cuba, and there was this
623 complete silence. (Shindell: Uhm-hmm.) This complete silence. It was embarrassing. And,
624 about two minutes later a guy who's in the very back row kind of leaned back in his chair
625 against the wall, put up his hand, and he said, "Bill, here in Cuba we don't have to do that."
626 [Laugh] I said, "Okay. Why don't you have to do that?" He says, "Bill, because at the end of
627 the year Fidel writes us a check." [Laugh] Okay? Moral of this story, for me at least, is that
628 unless you create a system where people have to make very hard decisions because capital is
629 scarce, unless you create a system where people have to define what they're going to do and
630 become the best in the world at doing it, (Shindell: Uhm-hmm.) then you spawn and
631 perpetuate only mediocrity. And so, I think that the Cuban system will be fairly good at
632 copying stuff that's been done elsewhere. They weren't the first to do streptokinase.
633 (Shindell: Uhm-hmm.) They were the first to do alpha interferon or hepatitis-B vaccine. But,
634 they won't ever create this critical mass of people that are so focused and so determined and
635 so able to transcend this kind of pseudo academic, pseudo commercial atmosphere that they
636 live in. So, I think the transformation that we're seeing in San Diego, to close the loop for us
637 here, (Shindell: Uhm-hmm.) is that you are seeing companies that are not only profitable and
638 very successful, they're very focused, they're cash flow self-sufficient, they're able to pile more
639 and more back into R&D. You know, these are the Biogen Idecs of the world, the Invitrogens,
640 the Amylins, the Illuminas of the world. So, that's the real, the real difference and hopefully
641 some of the smaller companies will learn from the business model that these people have
642 applied. I think all of them have really stuck to their knitting and have applied their capital in
643 a very focused, intense way towards single objectives that have gotten them to the point of
644 cash flow self-sufficiency, profitability, and growth. I think the mistake that an awful lot of
645 entrepreneurs make is they try to create their new companies in the image of Big Pharma that

646 they left last year, (Shindell: Uhm-hmm.) and they say, "Well, I need to deploy capital and I
647 need to diversify risk." Wrong. If you diversify risk across too many things, the way the
648 Cubans do it, (Shindell: Uhm-hmm.) okay, then you won't have enough capital to deploy in a
649 focused area to ever succeed. So, it is the investor who must diversify risk by investing in ten
650 companies. The company, small company, who invests in ten projects is doomed to failure.
651 (Shindell: Uhm-hmm.) And so, I think we are seeing the emergence of successful large
652 profitable companies here that will provide, you know, some of that model for how it was
653 done to the (Shindell: Uhm-hmm.) smaller companies who will take discovery out of
654 academia, become very, very development oriented, extraordinarily focused, and hopefully
655 become best in the world at their own little narrow niche (Shindell: Uhm-hmm.) in order to,
656 to succeed as cash flow self-sufficient companies.

657 **SHINDELL:** And this has been your, your business model and you've been pretty successful
658 with it. (Rastetter: Uhm-hmm.) Do you think that, that your example has had an influence on
659 the way that biotech is, is done here in San Diego?

660 **RASTETTER:** Hard to say. [Laugh]

661 **SHINDELL:** Hard to say? Okay. [Laugh] Let's see. Maybe I should just ask you now, you
662 know, what, what should I have asked you? What didn't I ask you that you would like to tell
663 us? Or . . .

664 **RASTETTER:** Oh, I think you did a pretty comprehensive job.

665 **SHINDELL:** You think so? Okay. Well . . .

666 **RASTETTER:** Thank you very much. [Laughter]

667 **SHINDELL:** Then let me ask you one last question. Is there anyone that you would
668 recommend we interview for this project?

669 **RASTETTER:** I'd interview Jay Flatley, who is the CEO of Illumina.

670 **SHINDELL:** Okay. I don't think we have him on our list right now.

671 **RASTETTER:** Okay. Jay has built Illumina into a very successful company in the genome
672 instrumentation space. (Shindell: Uhm-hmm.) And, I'm the chairman of Illumina, so I'm
673 biased, but I think it's a, [Laugh] I think it's a great company.

674 **SHINDELL:** Okay.

675 **RASTETTER:** So.

676 **SHINDELL:** Well, we'll put him on the list then. Is it F-L-A-T-L-Y? Or, is that . . .

677 **RASTETTER:** Yes.

678 **SHINDELL:** Yes? Okay.

679 **RASTETTER:** F-L-A-T-L-E-Y.

680 **SHINDELL:** E-Y? Okay.

681 **RASTETTER:** Yeah. Yeah.

682 **SHINDELL:** All right.

683 **RASTETTER:** Yeah.

684 **SHINDELL:** Okay. Then if there's not (Rastetter: Good.) anything else you want to add, I
685 think that would be the end of the interview.

686 **RASTETTER:** Good.

687 **SHINDELL:** All right.

688 **RASTETTER:** Good speaking with you, thanks.

689 **SHINDELL:** Yeah, it was a pleasure.

690 **END INTERVIEW**

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The San Diego Technology Archive (SDTA), an initiative of the UC San Diego Library, documents the history, formation, and evolution of the companies that formed the San Diego region's high-tech cluster, beginning in 1965. The SDTA captures the vision, strategic thinking, and recollections of key technology and business founders, entrepreneurs, academics, venture capitalists, early employees, and service providers, many of whom figured prominently in the development of San Diego's dynamic technology cluster. As these individuals articulate and comment on their contributions, innovations, and entrepreneurial trajectories, a rich living history emerges about the extraordinarily synergistic academic and commercial collaborations that distinguish the San Diego technology community.