

# Stan Fleming

*Interview conducted by*

*David Caruso, PhD*

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*Redacted transcript.*

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## Standish Fleming



A 27-year veteran of venture capital investing, Mr. Fleming has helped raise and manage six venture funds totaling more than \$500 million and has served on the boards of 19 venture-backed companies. He has extensive experience in all aspects of venture management and finance, including fund-raising, investor relations, operations and portfolio development. He has made investments, managed portfolio companies, raised funds, pursued business development, taken companies public and successfully exited investments through public-market sales and buyouts.

In 1993, Mr. Fleming co-founded Forward Ventures. In his capacity as a founding managing member he served as the initial president and CEO of Triangle Pharmaceuticals (acquired by Gilead Sciences, Inc. [NASDAQ:GILD]), Actigen (now part of Corixa/GlaxoSmithKline [NYSE:GSK]), GenQuest Corixa/GlaxoSmithKline [NYSE:GSK]), and CombiChem (acquired by DuPont [NYSE:DD]), and now part of Deltagen [Pink Sheets:DGEN]. Mr. Fleming was a founding board member of Arizeke Pharmaceuticals, CIPHERGEN Biosystems (now Vermillion, Inc. [NASDAQ:VRML]) and Gryphon Therapeutics, and formerly served on the boards of Acorda Therapeutics [NASDAQ: ACOR], Converge Medical, Doctors on Line, EndiCOR, First Dental Health, IntensiCare, Kemia, Inc., MitoKor, and Tandem Medical. He currently serves as a director of Ambit Biosciences [NASDAQ: AMBI], and was a founding director of Nereus Pharmaceuticals. Mr. Fleming serves as a director of CONNECT, San Diego's support organization for the academic-to-early-stage community, and is a past president of the Biotechnology Venture Investors Group.

Mr. Fleming enjoys extensive networks throughout the venture, entrepreneurial, scientific, medical and pharmaceutical communities. Venture funds he has managed

have made investments in more than 70 private and public companies, a number of which have gone public and/or been acquired by pharmaceutical companies. He has helped start more than 15 companies and served as founding CEO of eight.

At Forward, Mr. Fleming has made investments in almost every segment of the health-care industry, including pharmaceuticals, biologics, diagnostics, devices, services and software. He has managed both platform and product companies/investments in the portfolio and led or participated in financings at all levels from pre-start-up to PIPES in public companies, in both debt and equity.

Before establishing Forward Ventures, Mr. Fleming served as the chairman, president and CEO of GeneSys Therapeutics (merged with Somatix and acquired by Cell GeneSys [NASDAQ:CEGE]). He began his venture career with Ventana Growth Funds in San Diego in 1986. Virtually all the major investors in the Ventana funds were overseas corporations in the Nordic countries, Europe and Japan. While at Ventana, Mr. Fleming gained extensive experience helping limited partners realize their strategic as well as financial goals through the venture program. He earned his B.A. from Amherst College and his M.B.A. from the UCLA Graduate School of Management.

Source: Forward Ventures Website

**INTERVIEWEE:** Fleming, Stan

**INTERVIEWER:** Caruso, David

**DATE:** 12 June 2014

1 **Caruso:** Today is the 12th of June, 2014. This is David Caruso with Stan Fleming  
2 for a second session as part of the San Diego Technology Archives Project. Again,  
3 we're in San Diego, California. Last time, we were kind of getting into the early  
4 2000s, and I think that's what we're going to pick up and focus on today. Just to  
5 recap quickly, I believe what you mentioned was that with Forward Ventures IV,  
6 there was a greater focus on biotech and biopharma. Then you brought up with  
7 Forward IV, where there was a focus on the companies Ambit and Nereus. Is that  
8 right?

9 **Fleming:** Yes.

10 **Caruso:** I think you mentioned Forward V reflected a shift to products. But we  
11 really didn't have time to get into much detail about the evolution of Forward  
12 Ventures. So I think that is what we were really going to be focusing on today. So  
13 I'm going to turn things over to you.

14 **Fleming:** David, thanks for coming by and for the opportunity to continue the  
15 discussion or the monologue. What I wanted to talk about in this session is the  
16 evolution of the venture program at Forward Ventures as a venture company from  
17 about 2000 to the present. Much of the attention in the venture business is focused  
18 on the investment programs, and I think there's a widespread belief, even in the  
19 venture community, that the business is really just one of investing. People give you  
20 money, you evaluate opportunities, you invest money in those, you harvest them,

21 and it's all at the portfolio level. My interest has been as much or more at the firm  
22 level, even transcending the level of the portfolio.

23 So you have your individual investments. You have the collections of those in the  
24 portfolios, and you raise funds that build portfolios periodically, and then you have  
25 the overall program of managing a venture firm. As I say, most of the attention goes  
26 in at the portfolio-investment level. I remember talking to Duane Roth about a  
27 venture program he was thinking about sponsoring with CONNECT to work with  
28 pharmaceutical companies. Duane had support of some great entrepreneurs and  
29 good opportunities in town here but neglected to put any experienced venture  
30 managers or managers of the venture business into the program, just because it  
31 wasn't perceived as a needed element. Duane's background is as an entrepreneur,  
32 and certainly his capabilities as well as his experience at the company level were  
33 really outstanding.

34 My point there being that one as experienced as Duane either didn't feel it was  
35 necessary or didn't realize that this kind of experience [firm management] would be  
36 an important contribution to a management team. I got into that [firm  
37 management] perspective right from the outset in my business. When Ventana  
38 hired me in 1986, it was to work primarily on marketing the firm. So my early jobs  
39 were drafting offering memorandums, helping with the marketing, helping present  
40 [the firm]. So my first introduction to venture was really on the theory and practice  
41 of venture capital management rather than at the [investment] level, which is very  
42 heavily technical. At that time, we were doing both IT and biotech.

43 So as I evolved into biotech, I met Ivor Royston through Genesis Therapeutics, and  
44 then shifted my focus to biotech. I didn't bring a very strong technical background,  
45 but, finance and strategy were my specialties. That's an element of venture investing  
46 that I've always enjoyed. I think it's an important element in the development of  
47 venture. Some of the experience at Forward will illustrate and support that  
48 perspective. I think it's somewhat unique in the sense that most of the venture

49 people, if you ask them what they do or what the business is, most of the discussion  
50 is at the individual investment level.

51 So quick recap, I left Ventana in January of 1992, and helped Ivor with a little family  
52 fund, Forward Ventures, he had at that time. We talked about raising a larger fund  
53 with the help of our first million dollars from Sequoia Capital and some key  
54 introductions they made. We were able to get to a first close in on that first fund,  
55 Forward Ventures II, in April of 1993 on \$5 million. We ultimately ended-up raising  
56 12 and a half million dollars for that first fund, which was a very successful fund. The  
57 focus there was big science. Our most successful investment was Triangle  
58 Pharmaceuticals, which was the Burrough's Wellcome team. They developed a  
59 compound called FTC that was acquired by Gilead and became Emtricitabine  
60 [Emtriva] as a product. It is still sold today and is a very successful product for the  
61 treatment of HIV.

62 The Forward Ventures II was followed in 1996 by Forward Ventures III, which was a  
63 42 and a half million dollar fund. I was running the venture business. During the  
64 first fund, Ivor was full-time on the faculty at UCSD. In the second fund, which was  
65 Forward Ventures III, he was in the process of starting the Sidney Kimmel Cancer  
66 Center, and so that was his primary focus. Again, I was running the business and  
67 handling the details of due diligence and interactions with limited partners and  
68 whatnot. In Forward III, we were joined by Jeff Sollender, whom I had introduced.  
69 Jeff had come to see me in my Ventana days. Jeff had tried to raise funds for a  
70 biotech-oriented fund in Chicago earlier without success.

71 So he relocated out here. Jeff was doing individual investments for Bill Farley who  
72 was a major leverage buyout guy based in Chicago at the time. Jeff made a number  
73 of investments for him, and at the same time, he worked with us; helped us in  
74 Forward III. So I was full-time, Jeff was part-time between the Farley funds and  
75 Forward. Ivor was part-time between Sidney Kimmel Cancer Center and Forward.

76 In 2000, the three of us set out to raise Forward Ventures IV, and the timing just  
77 happened to be perfect.

78 *Caruso:* Dot com.

79 *Fleming:* The dot com bubble. We had our first close in April of 2000, and I think  
80 we had a final close in April of 2001. We were able to combine Jeff's track record  
81 with a number of the companies he was getting public and our track record. The  
82 timing was just perfect. The market peaked in March of 2000 I believe. There was  
83 plenty of money and interest in the institutional world for venture in general,  
84 biotech in particular. I can remember running to meetings in New York with Jeff in  
85 the back of the taxi, calling in to get the latest price quotes on our companies, and  
86 marking-up or at least discussing [with prospective investors] the step-up in  
87 valuations that were taking place literally in real time.

88 So it was a very heady time in the industry. We were very fortunate. I believe we set  
89 out – I don't have the numbers right in front of me – to raise 200 million. We ended  
90 up finally at 256 million. So when that fund closed, Ivor came on full-time. At that  
91 point, he decided there was enough substance to the venture business, and that's  
92 really where I think his passion was at that point. But it wasn't until we closed that  
93 fund that Ivor came on full-time. So it was Jeff, Ivor, and myself. We then brought  
94 in Joel Martin who – actually, I introduced Joel. Joel had been working with Kevin  
95 Kinsella, as an entrepreneur-in-residence and a venture member and that type of  
96 stuff for Avalon.

97 So Joel joined us. Then the three principals in the firm at that time were Ivor, Jeff,  
98 and myself. We invested that fund fairly aggressively. In retrospect, the funds that  
99 were the class of 2000 were the worst performing funds by vintage year in that entire  
100 era. It was the result of excess capital available; that's the nature of the venture  
101 business. But we were able to get that [money] in the ground fairly quickly. So the  
102 three of us, Jeff, Ivor, and I set out to raise Forward V with Joel, and then we later

brought on Stuart Collinson as well. We set out to raise the Forward Ventures V in the 2002 timeframe with Ivor, Jeff, and me as the principles, at that point.

We were approaching an initial close on that fund in late December of 2002, when Jeff was killed in an automobile accident here in town, and that left Ivor and myself. We were able to regroup and get to a first close in April of 2003. Clearly, we missed Jeff. He had been an early part of the firm, and he had a very unique perspective. He had a more public markets perspective, and it was a nice complimentary skill set. What I didn't appreciate at the time was Jeff's critical role in helping us with decision-making. So again, we get back to the dynamics at the firm level here.

Because Ivor and I were the managing members, it was our business. Stuart and Joel were employees along with the rest of the staff. Now they were employees of elevated stature, but still, they worked for us at our pleasure. So the principal decision-making process needed to take place at the senior level, which was initially Ivor, Jeff, and myself, though Jeff did not participate in the first close of Fund V.

In order to operate the firm, we [Ivor and I] each owned half of it at that point. We had to have an efficient decision-making process. Now Ivor and I are very different people, and that was the strength, but that was also a potential problem. Ivor tended to be rather compulsive. I had the finance and the management strategy background. Ivor has a technical background: science and oncology. He is a very impulsive decision maker. He tends to come to decisions rapidly right off the top of his head, and it's generally not a conscious, rational process for him, in the sense of starting with a data set and working through observations and conclusions and whatnot.

Ivor tends to be very spontaneous in his decision-making. It's not to say one [style of decision-making] is better than the other, it's just that they're different. The fact is that we could make a strong team because of the range of styles and strategies here. But as it turned out, and I didn't really appreciate it at the time, Jeff played a critical role in the decision-making process. Typically, when we came up against a



131 decision, often, Ivor would be at one end and I'd be on the other end, like balancing  
132 a teeter-totter. The farther out one went, the more one dug his heels in, the farther  
133 out on the other side the other partner would go in order to maintain the balance.

134 Jeff—in my vision—sat in the middle and leaned one way or the other. We [Ivor and  
135 I] both got along with Jeff; we had our differences, but Jeff was pretty consistent.  
136 Jeff's real focus was maintaining the value and the integrity of the business. I think  
137 we all sort of agreed with that. We might have disagreed with him on a particular  
138 decision, but as he leaned one way or the other, his focus and priorities were to  
139 maintain the balance and an effective working relationship there. When we lost  
140 that, Ivor and I really had no effective decision-making process. Worse than that, we  
141 had no way of working towards decisions.

142 I had this somewhat systematic kind of logical decision-making process. Ivor had an  
143 impulsive one. So I always wanted to de-convolute everything and look at each  
144 individual aspect and see if we could find something [common ground], and Ivor  
145 just had a decision. There was nothing more to talk about. It was just a yes or no  
146 kind of thing. So we really didn't have any basis for reaching a common ground. Ivor  
147 had always been part of the program up until then, but he had been totally focused  
148 on the technology, on the investment side. He really had no interest or no  
149 involvement on managing the venture firm. He just left that completely to me.

150 When he came on full-time, suddenly he had the responsibility. He'd always had the  
151 responsibilities because we were equal partners up until then, but in addition to the  
152 responsibility, he had the interest in the venture operation. Ivor was very interested  
153 in running, controlling the business. I didn't really expect that, because he hadn't  
154 shown any interest in that aspect of the business up until then. But once he came  
155 onboard, he became very interested in it.

*[18:33] Transcript redacted. Selection restricted through June 2025. [24:39]*

215 The long and the short of it [our new management arrangements] is that they [Ivor,  
216 Stuart and Joel] now control the Forward franchise. Again, I had responsibility for  
217 my board seats and my companies, and I participated and helped with the running  
218 the firm, but had no interest going forward in anything new. As I say, over time, that  
219 relationship became more and more constructive, and Stuart and Joel came to play  
220 the role of Jeff in the sense of helping break ties. You know, obviously I was  
221 concerned that it would be to my disadvantage, but, Stuart and Joel are basically  
222 business guys, and so they share certain common ground of what is in the best  
223 interest from a business and financial perspective. They agreed with me about as  
224 often as they agreed with Ivor, so that process worked. I say it got better over time  
225 as we were able to heal wounds and build trust, but it left those three without a  
226 dedicated venture fund/firm manager. They were very preoccupied with the  
227 portfolio investments, their own individual investments.

228 Venture firms tend to run in kind of two flavors: one being collections of individuals  
229 who invest individually and happen to share an office, and some have been very  
230 successful; and the other is more hierarchical in which you have more of a team  
231 approach where people bring different skills and everybody participates on each  
232 deal. There's a fundamental difference. That was my vision of the way a venture  
233 business should work, and theirs was much more in the silos. They were able to  
234 really exploit the silo model when I stepped to the side. At first, they were successful  
235 with Forward V. I mean we [they] were way ahead of the curve in that fund very  
236 quickly with early returns. We had one company [Proprius Pharmaceuticals], I can't  
237 even remember it, where we decided we weren't going to go forward with a funding  
238 and stepped back. It was a company we were invested with Atlas. They were able to  
239 find a buyer for it, and we ended up getting paid like two and a half times our  
240 money, and we had walked away. We hadn't even participated in the last round of  
241 financing.

242 It was just spectacular the progress they made with their focus on the portfolio  
243 companies as individual investors. At that point, they really were in a position to go

244 out and raise another fund. They could have written their ticket. Though the LPs  
245 were aware of the friction, we were able to solve it and at least paper it over. They  
246 appeared as a very strong investment team based on their track record. I think they  
247 were in a position to go out [without me] and raise another significant fund in the  
248 2007-2008 timeframe.

249 They didn't perceive that. They were working on the portfolio companies. They  
250 didn't see the long-term timing cycle for fund [raising] at the firm level. I kept  
251 waiting for them to go out. They never made a move, and they could have in the fall  
252 of 2007 through the first half of 2008. They could easily have raised a fund at that  
253 point. They missed that. We got into the second half of 2008, and I think everybody  
254 knows what happened at that point. There was the meltdown, and that precluded  
255 fundraising at the venture level at any point.

256 In the time between 2008 and 2010 or 2012 despite best efforts—it's just the nature of  
257 the uncertainty that's inherent in the pharmaceutical business—the portfolio saw a  
258 regression to the mean over time [closing the door on their ability to raise money].  
259 In other words, we were fortunate, we had early successes; then they were balanced  
260 by some losses, and less successful outcomes over time. So performance of that  
261 fund, which was well in the top decile early in the process, fell down to where we  
262 may be top quartile, on a given day, but I think we may have even fallen below that  
263 curve, depending upon the outcome of some of our current clinical trials. So the  
264 fund, as I say, saw a regression to the mean. The institutional money was not  
265 available. It became pretty clear that over time that fund was not getting stronger.

266 The lack of a follow-on fund in 2007-2008 made it difficult for us to look at new  
267 deals that might have been possible. So a lot of the time and effort then went into  
268 trying to maximize the value of our existing companies. They have struggled. We  
269 had setbacks in CancerVax, Favrilite fairly recently; so they didn't have a big impact  
270 on the fundraising in this time. About a year ago in the 2012-2013 timeframe, Tioga  
271 had a failed trial. The drug could have revived us. So again, the fund has struggled

272 since then. No fault of our own, just pharmaceutical development. But it left the  
273 firm in a position where it was really unable to access institutional money, and,  
274 barring some major changes here, [that] probably is still going to be the case.

275 When it became apparent that they were not going to be able to go forward, we let  
276 Joel go. Ivor and Stuart had worked on some things [raising new funds], and they  
277 may still be working on them. I have worked on a couple of schemes without  
278 success. I think the long and the short of it is that we were not able to raise a follow  
279 on fund to Forward V. Without fresh money and funding, the firm really does not go  
280 forward. We're in the process of scaling down the firm. We're finishing off the  
281 investments that we have. There's still some really substantial potential value in the  
282 firm, and the fortunes could change [but it is unlikely that Forward will continue in  
283 its present form].

284 I can't speak for Ivor and Stuart in terms of their plans at this point going forward.  
285 However, the thing that has come to interest me when I look at it at arm's length,  
286 over time, I think the failure of Forward to build a long-term franchise in the bio-  
287 venture industry really stems from an inability to manage the human capital that we  
288 had. We had some extraordinary human capital in the partners. The inability to  
289 operate as a team, the decision of the three to work in a siloed fashion, and in that  
290 format, the inability to bring a broad range of disparate perspectives to bear on the  
291 venture process meant that decisions were made without the full benefit of the skill  
292 set that we had.

293 The specific thing [missing] in the skill set was again, a real focus or experience at  
294 managing venture firms. I mean I had been in the venture firm management since  
295 1986. As I said, I started on the administration rather than on the portfolio side, and  
296 so by 2003, I had 17 years or so experience in that area. None of them had ever run a  
297 venture fund. I was sort of disappointed. I thought Joel might have had more, but  
298 he was at the portfolio/investment level with Avalon. Certainly Ivor and Stuart had  
299 never run venture funds. So I think that that lack of experience and a lack of

300 appreciation for what was missing at that level resulted in missing the critical  
301 opportunity to go forward.

302 The first rule of managing a venture business is when money is available, take the  
303 money. [Biotech portfolio companies are running clinical trials.] You're running  
304 clinical trials. You're going to wake up the next day and find you've had a death in a  
305 trial, and suddenly your flagship project is worth nothing. So the firm ended in  
306 neglecting the basic rules of operating a venture firm, and it paid a price for it. It's a  
307 shame. I don't see that it needed to happen, but, in retrospect, one becomes  
308 resigned to it, and it's interesting to contemplate at a distance. [The mistakes  
309 involve] a lot of the basic rules of business of leadership, of team building, and all  
310 that, [the stuff] that venture guys love to lecture [their companies] about.

311 That our inability to execute in those areas [resulted in] was really a failure of the  
312 business isn't exactly a fair characterization, because Forward has had a very  
313 successful career. We've developed some very important products and companies.  
314 We've made nice returns, certainly, in a number of cases. However, you get older,  
315 like Ivor and I are – like I am, anyway, you look back on what could have been,  
316 should have been, and would have been. That's one area that I think that could have  
317 been much more than it was, when we were ahead of the curve or they were ahead of  
318 the curve in the first say three to four years of that fund [Forward V] before it  
319 regressed to the mean. Now they're in danger of falling behind the curve because  
320 the other funds that did raise money in that timeframe made investments in the  
321 time between 2008 and 2012, [which proved to be a very good time] in the venture  
322 business, as opposed to the 2000 vintage fund where capital was plentiful and too  
323 many companies got funded. In the last half of that decade few investments were  
324 made [2008-2012]. The reduced supply of companies and supply-and-demand  
325 pricing [made venture investing] more effective then. The other element of it is  
326 that—what people didn't anticipate—was the window opening up in the public  
327 markets. The amount of liquidity that is available in the industry today, starting  
328 about 2012, or certainly '13-14, is absolutely staggering. It certainly far exceeds

liquidity I think at any time in the history of the bio-venture industry. Obviously there is a sharp contrast between 2014 and 2000.

Probably the toughest time of all was when the venture guys went off to chase the internet and stopped investing. The big guys in Silicon Valley, including Sequoia, our sponsor, Kleiner Perkins, and Accel—groups—we had really depended upon them for follow-on funding—[stopped investing in biotech]. That was the absolute worst. But in 2008 going forward, there was virtually no new money. Fortunately, the industry [but unfortunately not Forward] had filled-up [on capital] before then, so they had reserves to get them through. Then the window opened up as a result of the Federal Reserve pumping all this money into this system. Really nothing happened in the venture business for years. Suddenly, the industry was awash and still is to some degree with capital in the public markets.

That changed the landscape entirely, and the venture funds that were positioned to take advantage of that influx of capital in the public markets were the ones that benefitted. That's the new generation that's going forward, similar to the way we were able to benefit from the 2000 window that opened up. Now a lot of venture funds like ourselves got left behind. But again, with a 2007-2008 fund, it would have been opportunistically positioned for a repeat of the 2000 kind of window opportunity. Missing the opportunity to raise funds in 2007 meant that we weren't positioned to take advantage of the next window that came open here in 2012-2013.

The result is that we continue to fall behind the curve in terms of access to capital, which is unfortunate. But again, it stems from that fundamental focus on individual portfolios among the partners at the company level rather than managing the venture business.

**Caruso:** So a couple of questions about this. One question about this period of time more specifically, and then a couple of general questions that follow on. The first is, in this span of time from 2002, in the various future ventures, were you

focusing on companies that were—not necessarily similar—but in a certain area of science?

**Fleming:** Yes. You raise a good point, David. The bio-venture business has always been a business in flux in the sense that there has been no overriding business model that has been vetted and proven to be effective and can be relied on to provide the levels of returns that are required for institutional investors. I think there's somewhat of a contrast between life sciences and IT in that regard. In the early to mid '90s, the focus was on big science. In fact, through the '90s entirely, Sidney Brenner, one of our advisors, used to refer to these areas of basic biology as the "omics:" genomics, proteomics, and those sort of large-scale science things.

I think we were relatively successful in that space. But those large-scale platform companies did not pay out in the public markets. The public got burned significantly in investing in those companies. For instance, our genomics company was called Sequana that we did with Avalon was in major competition with Millennium, and both failed as genomics platforms. Millennium was able to even license some compounds and ended up doing fairly well. We had a combinatorial chemistry company, CombiChem.

Starting in 2000 going forward, as the industry evolved some [venture firms] went into platforms; some went products. We went into products, which I think was overall a good strategy. However, neither Forward nor many of our venture colleagues had a lot of experience really working in pharmaceutical development, and so it took a while to get the learning curve going in that regard. You're in a high-risk business when you're in the business of developing pharmaceuticals and returns are based on clinical trial results.

So I think that the 2000 fund in that vintage suffered from this transition from science to platforms and products, and the industry was really at a disadvantage in all three of those sectors. The 2003 fund was more focused on products. We were able to get access to products that were farther along or closer to the clinic, and in

384 some cases in the clinic. Those funds, at least potentially, fared better than the 2000  
385 vintage, though again, subject to this high pharmaceutical development risk. In the  
386 2007/2008 funds, again, we were not active. We didn't have a fund at that time.

387 Companies that have done well in that space have tended to be product-based  
388 companies with some platform work, but primarily product. You know, given the  
389 nature of the pharmaceutical development, the unpredictability of these outcomes  
390 and whatnot, having more entries in the process was a significant advantage in terms  
391 of finding products that really paid off. So having a narrow portfolio in that  
392 environment was a significant disadvantage. The 2007 groups were able to have a  
393 broader range of opportunity and options, and as a result, had more success with  
394 product-based companies when the window came open.

395 So it evolved. We were not optimally positioned to take advantage of that. Also,  
396 over time, the venture industry, both individually and collectively, became much  
397 more sophisticated in pharmaceutical development. We were not in a position to  
398 draw on that. Some of that is the result of substantial layoffs in the pharmaceutical  
399 industry, which made incredible talent available in the entrepreneurial and venture  
400 markets, but that process really didn't start until 2008 or so. So again, we did not  
401 have the benefit of that skill set that other venture groups with those later funds did.

402 **Caruso:** So part of the reason I wanted to ask that question is – and I know this is  
403 kind of a chicken and the egg sort of question—is I'm curious to know your  
404 perspectives on what you think overall the VCs influence on the trajectory of science  
405 happens to be. I could see it as two things. There are a lot of companies that are  
406 interested in a certain sector, and so VCs are going to move towards supporting  
407 some of those companies because in some ways, science is defining the way that it  
408 wants to go. But I could also see VCs coming in, saying, "You know what? There's a  
409 whole group range of companies out there. The ones that are doing cancer vaccines,  
410 for example, are the ones that should be invested in."



411 In some ways, VCs because they're investing in those companies and not others, they  
412 could also potentially be pushing science to a specific direction. So I'm wondering in  
413 your experience if you've felt that you were in some ways or VCs in some ways were  
414 defining the areas that science was going? Or is it more of just that this is the general  
415 area that everyone seems to be, and you're following where the trend in science is  
416 going on its own?

417 **Fleming:** You know, the short answer is yes, both processes work. I think from  
418 the venture perspective, there's more of a feeling that we follow science rather than  
419 dictate science, because we tend to see ourselves as opportunistic and responsive to  
420 opportunity as it comes in. One of the things that I think – I don't know, maybe  
421 some venture guys would argue with me—is that there's always the old expression of  
422 the drunk looking for the keys under the lamppost because that's where the light is.  
423 If you come to science or the life sciences with a preconceived shopping list, you're  
424 going to miss a lot of the good stuff that you hadn't anticipated. What we're talking  
425 about here is this unpredictability of both the science and the clinical development  
426 side, and the venture guys want to be in a position to take advantage of it as it rises.

427 Then also, there is the unpredictability of business opportunities because the  
428 pharmaceutical industry is a very dynamic industry. So assets are always being  
429 traded and turned over, and you want to be in those streams as well. That said, the  
430 ability to advance science in general – and the question of whether it's applied  
431 science or pure science is getting to be more and more blurred as you go on—clearly  
432 the more capital that's available for applied science or science applied in particular  
433 areas, the more data that's generated, the more information, the more opportunity  
434 there is. So I think there is a feedback loop there to some degree.

435 I can remember in the early days, back in the early '90s, when we were first getting  
436 started, Ivor and I, there was tremendous concern at the academic level that venture  
437 – that commercial money in general, venture money in particular – would co-opt the  
438 integrity of the scientific community, the academic community. Financial rewards

would distort the selection of projects and science and whatnot. I think that's much abated. In fact, what people have found in the meantime is that there may be some of that to some degree, but really what venture in particular and pharma as well has done for science and the academic community is much more complimentary than competitive or preemptive. So it has enabled scientists to broaden their spectrum, to do things that they wouldn't otherwise do, particularly now in this era when we're seeing substantial cutbacks in the NIH and stuff. In a lot of ways, it's a life-ring for some of these guys, the academic scientists. I include pharma in that as well.

I remember in the old days, I'd say, "Okay, you have a project that you think is worthy of commercial development, and we're here to fund the commercial development. What can you do? What can we do?" The rule was that they [the scientists] could get funding [from the government] only to cure cancer in mice. If it went beyond mice or maybe dogs, there was no NIH money for that at all. That was purely commercial, and so that's essentially in a simplistic manner how we divided up the world with those guys.

In that environment, the scientists were quite interested in seeing their discoveries tested in humans. In fact as it turns out, I think they probably appreciated that—maybe even more so today—that humans are a different ballgame from animals. If it was a question of curing cancer in mice, we'd have cured cancer a long time ago. [Humans are] It's a heterogeneous population. It's out-bred. It's complex. The organism is much more highly developed [evolved]. Applying scientific principles, basic science, to the treatment of disease in humans has turned out to be a very complex, very fascinating, very interesting science in itself. I think that the academics feel that they've benefitted from, if not actually participating, at least observing that, and seeing the work being advanced into those areas, which they couldn't have done under the old regime.

So I think most of that work has probably been more complimentary than as I say competitive or preemptive. Still, we've got to keep things in perspective. The

467 venture business is a very small slice of the commercial world, the scientific world,  
468 and very uniquely focused on specific kinds of deals. We're really quite limited in  
469 the kind of things we can fund, and you know, our appreciation [of our limitations]  
470 over time has evolved. We've become more and more limited in our perception of  
471 our capabilities in the face of the kind of challenges that pharmaceutical  
472 development requires.

473 Really, in most cases, the venture business sees itself as a bridge, a conduit from  
474 academic to commercial or from academic to the mainstream pharmaceutical  
475 industry. So in that regard, I think the real bulk of the influence of the commercial  
476 world on the direction and development of academic science is driven by the  
477 pharmaceutical industry. One of the things that has happened over time with the  
478 venture guys is as we've taken in a lot of these people that were laid off, or not even  
479 laid off, just people in the pharmaceutical industry who were more interested in an  
480 entrepreneurial environment. Whether it's at the level of a fund or a portfolio  
481 company, the industry has become more and more aligned with the needs and the  
482 requirements of the pharmaceutical industry. At the end of the day, that more than  
483 anything is driving the direction of applied science in this space.

484 **Caruso:** I actually think you spoke to part of my third question, so it may be  
485 pointless in asking it. I was also just thinking about the role of VC. I've spoken with  
486 some other individuals who are talking about investing in [early-stage biotech]. In  
487 the early years, they would take a lot of time to do their own research to meet with  
488 the principles of a business to decide whether or not to invest, but now they actually  
489 rely more on the VC analysis. If a venture capital firm is interested in some business  
490 or some group of businesses, other investors that might be coming in later or  
491 coming in as add-ons, now turn to the VC analysis as the source of expertise in terms  
492 of whether or not a company is worth funding scientifically or from just purely a  
493 business perspective.

Like I said, I don't know if there's really a question in there, but it's something that I've heard people note, and I think you've spoken to that a little bit where, in some ways, you're establishing a certain level of expertise because of your investment in these companies. In some ways, you're validating them to a certain degree beyond just your own interests.

**Fleming:** Sure. You know, that's always been the case, and that's even more so today, and I think for a couple reasons. One, we're seeing a greater availability of capital in both the public and the private markets, but also a broader availability. More different sources, more high net worth individuals, foundations, disease foundations, like the Multiple Myeloma Society. People like this are participating in biotech company formation and early financing that [they] never did before. At the same time, this evolution that I talked about in terms of the venture community and how Forward sort got on the wrong side of that, got behind the curve, we were certainly not alone in that regard, as you know. I think the number of firms today that are active in the venture investing, certainly the mainstream groups is less than half of what it was back in 2007.

So there's been a tremendous contraction. Now if you look at the amounts of money raised, I don't have the numbers exactly, but I think we're certainly seeing a rebound, the renaissance in that regard, and I would expect that capital raised by venture funds for investment in life sciences is probably comparable if not greater than what was available in the pre-meltdown era. The difference is that more and more money is going into fewer and fewer hands, and that has a profound effect on the nature of that private market. So the more players – if you have a lot of players bidding on assets and whatnot, you tend to have a more efficient market in terms of pricing and competitive market and whatnot.

As you have fewer groups, as you approach one single investor, the market characteristics really change from a competitive market to a club. The dynamics of a club are considerably different than an open market. An open market is

522 competitive. A club is cooperative. “You do my deal, I’ll do your deals. If we’re all in  
523 the deal at the outset, then we’re not subject to competitive pricing. Later when we  
524 come back to market, we will have with a lot of money around the table – and  
525 biotech is very capital intensive; we will have substantially reduced the financing  
526 risk.”

527 A lot of the companies that have been lost in the past, and some even in our  
528 portfolio, were lost for want of capital. You know, technology worked well, but you  
529 just weren’t able to raise the funds. So if you can take financial risk off the table,  
530 that’s a significant advantage. It doesn’t eliminate pharmaceutical risk, which is still  
531 very high, but at least you’re better off in that situation. So you tend to see much  
532 more of a club mentality here, and what that creates is that if you’re in the club, if  
533 your portfolio company is in the club, it has tremendous access to resources, capital  
534 people, support and whatnot.

535 If you’re not in the club, you have much less access. You have a have-and-have-not  
536 kind of situation. So in that sense, I can understand what the venture guys are  
537 doing, because those mainstream venture-funded companies have a substantial  
538 advantage in the private markets. You have better access to the public markets,  
539 pharmaceutical industry, and all of these things. The experience and the franchise  
540 that these guys have tend to keep the industry narrow and keep people out. But, I  
541 think that looking to see how opportunities are vetted and perceived in the venture  
542 community is probably a critical element for other groups – the foundations, high  
543 net worth individuals, and whatnot – in evaluating the crowdfunding opportunities.  
544 Generally, even the foundations, may be technically sophisticated about how to treat  
545 a disease or the nature of disease, but they’re certainly not experienced in any  
546 commercial development aspects.

547 The venture business really requires a very broad base of experience. We talked  
548 about experience and the breadth of experience really required to run a venture  
549 fund. There is the same or greater breadth of experience at portfolio companies.

That's why team building is important. You have clinical, you have legal, you have operations, and it just goes on and on and on. All that expertise needs to be integrated and coordinated in a team-oriented fashion. So the venture guys really bring an extraordinary resource to the table. It's going to be very interesting to see if and when the Fed [Federal Reserve] does turn off the spigot or take away the punch bowl, as the expression goes, and capital becomes less available, whether a lot of these companies that are started outside the venture mainstream – by foundations, family money, or whatever, bootstrapping, entrepreneurial bootstrapping – whether you're going to see a major washout in that area, which would then discourage this kind of entrepreneurial participation and really restrict the focus to the mainstream venture guys, which would seriously limit the availability and supply of companies and products to the pharmaceutical industry.

**Caruso:** I don't have any other questions. Are there other things that you'd like to discuss?

**Fleming:** No, just to sort of sum up, bio-venture, life sciences venture has always been interesting, and is more interesting and exciting today than it has ever been in the past. It is still in evolution. It is a substantially smaller, but better funded industry today than it was ten years ago. It continues its quest to find sustainable business models. It remains to be seen [where it will lead.]

We have groups like Third Rock in Boston that are doing these large scale platform deals. Actually, the head guy there is a guy named Mark Levin. Mark was the CEO of Millennium, and a lot of the stuff that they're doing at Third Rock is a recapitulation of the Millennium plan. Now I don't think any other venture groups have been able to sustain that model, make it work, but Mark (a) was very good at it, and (b) he has much more active support from the pharmaceutical industry today than we ever had in the past. So maybe things are going to change in that regard. Again, [the large-platform model is still] unproven; it remains to be seen whether the very limited number of practitioners in that large scale model [can make it work].

At the other end of the spectrum are groups like Atlas, and here in town, Avalon that are doing these completely virtual product-oriented companies. I don't know if it's traditional, but it's a very different business model that they're testing. Then overall, this is a very heady time in the industry because capital is readily available. If you look back over the times when capital has been available in the venture market, [you see] a couple things; we had windows in, 1990-91, 1995-96 and 1999-2000. Those were times when money was available, and it almost always correlated with the Federal Reserve using monetary policy [to increase the money supply].

When enough money comes into the market, some of it eventually finds its way down to the life sciences. We're kind of the last guys, bio-venture, the last guys in the pipeline. The money [?] has a tremendous effect because biotech is such a capital-intensive industry. Today, the Federal Reserve has pumped money into the system at an utterly unprecedented rate, and money has finally trickled down to the life sciences at an utterly unprecedented rate. So it just seems long-term, that's going to be unsustainable. It's never been sustainable in the past. Maybe the Federal Reserve can continue to print money forever, but I think the conservative assumption would be at some point, the money is going to dry up. When that happens, how is the industry going to respond?

I think the mainstream venture guys will do okay. They're experienced, have good access to capital, and have good support from the pharmaceutical industry. They have good institutional relationships. So I think those guys are going to be okay. They also have a limited supply [of companies] and a virtually unlimited demand, both from pharmaceutical companies for the products that they can't seem to develop themselves, and from the healthcare market with unmet medical needs.

I think they are in a very good, long-term position, and so it may be sort of a golden age of venture. In that sense, it's sort of a shame to miss that curve, but some days you make it, some days you don't. The long-term perspective for the industry is still uncertain. These are unproven business plans. At the end of the day, if the venture

guys can't provide the returns that the institutional guys need, they're not going to continue to provide them money.

Then the question is the long-term survival of the pharmaceutical industry. You know, they're facing potential price controls. Large-scale price controls will kill the venture business and severely damage the pharmaceutical industry, and limit innovation. Innovation is what the venture industry has to sell here. The venture industry has never had—as I say—a standard or a proven operating and investment model. The conditions look better today than they have looked in the past. Whether the whole combined venture entrepreneurial and pharmaceutical communities can meet the needs for of the healthcare system and of the patients and can really fully or adequately take advantage of and exploit the scientific breakthroughs that are coming even ever faster every day remains to be seen.

That's an interesting question. I tell you, it's been fascinating watching it from our perspective here at Forward and from my own. Stay tuned. It's very much an industry in flux. Specifically how that affects this community really remains to be seen. The real strength of San Diego is basic research. We don't really have operating, large-scale pharmaceutical companies here in town. A number of the major pharmaceutical companies have a presence at a research and early development stage here: J&J, Pfizer, Novartis, and Lilly, and so on.

Early stage development has been a challenge for both pharma and venture. If we can't improve the efficiency of early stage development – getting [more] compounds into late stage development – that's going to be a real threat to the future of this community. If we can improve the efficiency, the partnership between pharma and venture and entrepreneurial community, San Diego probably has a very bright future because our research community is outstanding. Our ability to generate opportunity, scientific opportunity, is as good as any [region], and better than most, as they say. But pharma and venture together have to figure out a way to be more efficient in that regard, or it's going to become a real stumbling block.



Also, San Diego's position on the Pacific Rim and our access to Asia and whatnot is another absolutely key element. That's one I think the SABPA [Sino-American Biotechnology and Pharmaceutical Professionals Association] group would be interesting to speak with. But again, this question of where is China going. You know, if the big guys [China and the US] have a fight in the elevator, the little guys are the first guys to get trod upon. What are we capable of – what can be sustained in terms of Asia? The nature of that opportunity remains to be seen and is sort of evolving.

Innovation is the key to being able to grow first-world economies, advanced economies. An economist was saying it's between 60 and 80 percent of the growth of an advanced – the first world economy comes from innovation, and innovation is absolutely essential for the future of the pharmaceutical industry because of the patent expirations and the challenges that they need to continually replace these products. [To the extent] that San Diego, and California in general and the bio-venture, biotech community are focused on innovation, I think they're absolutely at the center of where the industry needs to be and has to go. The fact is that innovation is exploration, invention. There's a fundamental level of uncertainty that is very difficult to manage in a commercial environment. We need new business models; we need entrepreneurs and whatnot, and how we're going to get from here to there really remains uncertain. But the fact is that we're in a great position to run those experiments, to test those opportunities and ideas.

It's absolutely essential that business, science, healthcare systems figure out these kinds of solutions, but there's no guarantee they're going to do it. You could easily come up with some very dark scenarios here based on limited healthcare budgets. I mean look what's already happening to the academic research community as a result of cutbacks of the federal government. I think it's highly likely that those are going to continue and are going to increase. The federal government has made it very clear that they are shifting their priorities from basic research to real-time consumption, and there's only so many dollars out there.

663 If the federal government, which ultimately is the payer, can't afford to pay pricing  
664 and reimbursement for these new technologies that justify the investment, they're  
665 not going to happen. So there's some real challenges here. It'll get quite interesting.

666 **Caruso:** Yes. Scientists at many academic institutions are there only because of  
667 government grant.

668 **Fleming:** Absolutely.

669 **Caruso:** The institutions don't pay the scientists really. It's the grants that do.  
670 So if the grants are gone, there are no more scientists producing science, and also no  
671 more individuals training the next generation of scientists.

672 **Fleming:** Absolutely, David. We are the beneficiaries of a tremendous investment  
673 that's been made since the World War II in this space. We [the US] have built a  
674 research community, and an intellectual space and momentum that are unparalleled  
675 in the world. If we fail, there isn't anybody who is going to pick up the reins and  
676 continue the process. So it's critical that we find ways to do that, but if the US loses  
677 its nerve, if it falters, it will – we will – pay a very high price for that.

678 You know, when I talk about the federal government providing the conditions that  
679 enable people to make the kinds of returns that justify investment in pharmaceutical  
680 development and discovery, that investment includes the research at the front-end  
681 to create the opportunities. It includes the pricing and reimbursement on the other  
682 end to pay off specific investment. You know, this big uproar about Gilead's  
683 compound Sovaldi – the problem isn't that it's not fairly priced. It's \$84,000. It's  
684 probably less than the overall cost of treating a patient today. However, it's paid in  
685 one year where the overall cost [without the drug] is realized over a lifetime, albeit a  
686 shorter lifetime, with existing technology.

687 The concern is that bolus, that threshold, of cost that the system has to get over in  
688 order to realize the long-term benefits of a cure versus a chronic treatment may

689 exceed the [current] health-care budget. If the US can't pay for it and they clamp  
690 [down] – they set price controls or whatever – “here is all we can pay, this is all we’re  
691 going to give you” – you’re going to see the money available for early-stage  
692 investment dry up. There’s not a lot of money going into early stage investment  
693 today even now. Sure, there are family, friends, foundations, and whatnot, but if you  
694 look at the pharmaceutical industry, they’ve cut back tremendously on their early  
695 stage R&D. You look at the venture guys. Sure, there’s plenty of money in the  
696 venture business but fewer funds, and in those areas, only a small minority of those  
697 venture funds do the early-stage work that is needed to take technology from an  
698 academic lab into the commercial development stream.

699 The tragedy of all that from my perspective is that if we really do fall short on our  
700 commitment and ability to develop new drugs, no one is going to notice it. It’s going  
701 to be opportunity costs. It’s going to be new drugs, medications, and therapies that  
702 didn’t happen. The fact that we could have cured cancer, we could have treated  
703 Alzheimer’s, it just will be lost in that.

704 I loved Larry Goldstein’s comment when they were putting CRM into place, you  
705 know, the Center for Regenerative Medicine. Early at the outset of that, there were a  
706 whole bunch of lawsuits that held up the allocation of those funds. Somebody asked  
707 Larry what was the effect of these lawsuits in holding up the thing. Larry said,  
708 “Look, it’s going to take us 15 years to develop new therapies, fifteen to 20 years to  
709 develop new therapies based on stem cells and whatnot. If you start that today, you  
710 get it in 15 years. If you start it five years from now, you get it in 20 years.” That  
711 same sort of logic applies here. If we don’t start on these [new therapies], if we don’t  
712 have the money to do them, they just aren’t going to happen.

713 So it’s a very exciting time, capital flowing freely, and opportunities, and excitement.  
714 Every day you pick up a newspaper, there’s a pharma merger, there’s a new product,  
715 and all the rest of the stuff. At the same time, there are a lot of really basic questions  
716 that this industry faces. You know, I’m spending a lot of my time thinking about this

717 and writing about things like that, but so there's a bit of wishful thinking here. I  
718 don't have an interest in – well, I do – participating in a venture fund, but my real  
719 interest in a venture fund going forward is much more at the firm level, and rather  
720 than the actual sleeves-rolled-up and hard work of that.

721 I think that that's a shame. I miss not having a second generation to [to whom we  
722 can] hand-off this [franchise] and the benefit of not only our experience and  
723 wisdom, if I may use the word, but the resources and the relationships and whatnot  
724 that we've built here. But that's life.

725 **Caruso:** Yes, all right. Anything else?

726 **Fleming:** That's a dangerous question to ask me, David, but at this point, I'm in  
727 good shape. Again, I appreciate your patience and the opportunity to talk with the  
728 archive, and I certainly wish you guys in the program well.

729 **Caruso:** Thank you very much.

730 **Fleming:** I think it's a fascinating time. I think you're talking here industrial  
731 revolution type stuff – maybe the bio-industrial [revolution], and I think people are  
732 going to look back, and they're going to be interested to see [what we did]. Of  
733 course, when you look back on these things, it looks like it was obvious. When the  
734 venture guys figure out how to do this and pharma [learns] how to really innovate,  
735 well duh. But you know, when you look at it from where we are today, it's not nearly  
736 as clear.

737 **Caruso:** No, and that's why we're capturing it. So thank you again for  
738 participating.

*[End of Audio]*

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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.