

FOURSQUARE PARTNERS

Company: Medivation, Inc. (MDVN)

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I have reviewed five year-old Medivation (the "Company") as a short thesis based on its 1) too-good-to-be-true observation regarding Dimebon's clinical activity in Alzheimer's disease ("Alzheimer's") and 2) its elevated market capitalization of \$682 million based on 30.0 million shares outstanding at \$22.72 with \approx \$230 million of cash and equivalents at year end. The major risk to the short thesis lies in Medivation's lucrative, high profile, September 3rd deal with pharmaceutical behemoth, Pfizer.

Conclusion: Medivation has in-licensed Dimebon to treat neurological disorders such as Alzheimer's and Huntington's disease ("Huntington's"). Dimebon is an over-the-counter antihistamine used in Russia for more than 25 years. Medivation has published stunning results from what the FDA has deemed to be a "pivotal" Phase 2 trial in 183 Russian Alzheimer's patients. Last June, the Company initiated a second pivotal trial, this a bona fide Phase 3 trial, in 525 patients. Medivation will conduct this trial in the US, Europe and South America. In September, Medivation struck a \$725 million partnership, including \$225 million paid up-front, with Pfizer. Medivation is also in a Phase 1/2 trial of a drug to treat prostate cancer. After reviewing the relevant literature, I believe there is little or no chance that Dimebon will demonstrate efficacy in Alzheimer's or Huntington's, supporting a short thesis. Only an acquisition of Medivation, e.g., by Pfizer, within the next 24 months, will prevent a massive loss for shareholders.

Medivation

Headquartered in downtown San Francisco, Medivation was founded in September 2003 by President and CEO, David Hung, MD and CFO Patrick Machado, JD. In October 2003, the Company acquired the rights to Dimebon for neurodegenerative disease or anti-aging purposes. The Company paid Sergey Sablin, Ph.D., operating under his home-based company named Selena Pharmaceuticals, Inc., \$25,000 in cash plus the equivalent of 2.2 million shares of common stock. In December 2004, Medivation came public by a reverse-merger into a publicly-traded, so-called blank check company named Orion Acquisition Corp. II. At March 1, 2005, Selena's beneficial ownership in Medivation was almost 19 percent, Dr. Hung's was 14.7 percent and Mr. Machado's was 4.9 percent. Finally, entities affiliated with Austin Marx and David Greenhouse of Special Situations owned almost 27 percent.

Dimebon

Around 1983, Dimebon (trade name for dimebolin) was launched in Russia as an over-the-counter oral antihistamine to treat allergies, itchy skin and so on. It does not appear to have ever been a prescription drug. In February 2001, the US Patent Office issued patent #6,187,785 which described Dimebon's potential utility in Alzheimer's and other neurodegenerative disorders. The patent was assigned to Selena Laboratories. The patent emphasized Dimebon's activity as an NMDA receptor antagonist (**N-methyl-D-aspartate**). This is the same target/mechanism of action as Forest Laboratories's Namenda (memantine) which was FDA cleared in October 2003 for moderate-to-severe Alzheimer's.

What is surprising about proposing the utility of Dimebon in neurodegenerative disease is that it is, biochemically, much better as an H-1 receptor antagonist, like other antihistamines, with an IC₅₀ of less than 50 nanomolar, than it is as an NMDA antagonist with an IC₅₀ of \approx 84 micromolar. These values can be found in Medivation's May 2, 2008 8-K filing. Simply put, this means that Dimebon is almost 1,700 times less potent as a member of the Namenda drug class than it is as an antihistamine. See below for how Medivation has side-stepped this inconvenient issue.

For more than 30 years, Dimebon appears to have been a solution in search of a problem. A casual review of the Dimebon literature is useful. One of the earliest references I found, November 1971, notes the benefits of Dimebon on *bacterial infection* in animal models. A September 1983 paper described the ability of Dimebon to increase survival in rats and mice at risk of dying from the shock associated with *severe burns*. Dimebon showed *antiarrhythmic* activity in rat, rabbit and dog assays in an April 1995 paper, leading the authors to conclude that the drug "...be recommended for submission to clinical trials..." for this indication. And, when dosed intravenously, Dimebon exhibited moderate *coronary vasodilator* activity with little effect on myocardial contractility in dogs and cats, which the authors concluded was a "...beneficial cardiotropic effect..." in their February 1996 publication. But wait, there's more. In July 2006, in vitro experiments enabled researchers to conclude that Dimebon has *anti-aging* properties.

Thus, while Dimebon seems to have demonstrated any number of intriguing activities over the past twenty-five years, Medivation has focused on its potential to treat neurodegenerative disease, especially Huntington's and Alzheimer's. Since the initial premise for Dimebon's activity as an NMDA antagonist in Alzheimer's appears weak, Medivation and its advisors have proposed a novel mechanism of action to explain the drug's observed activity in clinical trials.

The underlying cause(es) of Alzheimer's are actively debated. At least two hypotheses dominate, an older hypothesis has been discounted and Medivation's is a fourth. Despite progress in the field, the only method to confirm a diagnosis of Alzheimer's is by brain autopsy, after death. When viewed under a microscope, brain tissue from an Alzheimer's patient exhibits (Theory 1) *extracellular plaques* composed of beta-amyloid protein and (Theory 2) *intracellular neurofibrillary tangles* made of tau protein. There are data that support and refute each theory, especially with regard to cause and effect. The third and weakest hypothesis suggests that Alzheimer's is caused by decreased synthesis of a neurotransmitter, *acetylcholine*, in the brain. Four of the five FDA approved drugs for Alzheimer's (e.g., Pfizer's Aricept, Novartis's Exelon) inhibit acetylcholinesterase which effectively increases local acetylcholine levels, but they show very modest efficacy in Alzheimer's symptoms or progression.

In May 2003, Bachurin et al. (including Dr. Sablin) published in vitro data indicating that certain drugs, including Dimebon, can prevent the inappropriate opening of mitochondrial pores due to neurotoxins, e.g., beta-amyloid. Thus, Dimebon could preserve mitochondrial function in neurons. The assay used to measure mitochondrial pore opening was crude and the mitochondria used were isolated from *rat liver*, not brain; however, the authors found that cyclosporin A -- the immunosuppressive used in organ transplants -- was 100 times more potent than Dimebon. Perhaps due to the crude assay used, Dimebon had to be tested at a fairly high concentration of 200 micromolar versus cyclosporin at 2 micromolar. This would translate to bucket-loads of Dimebon in a human. Medivation's Dr. Hung has suggested that the Company's more sensitive assays have found Dimebon to be active in the low nanomolar range, a thousand times lower. If that were the case, then cyclosporin might be active in the picomolar range, another thousand-fold lower, to prevent Alzheimer's.

And, if this were true, cyclosporin which is cheap, generic and has a large safety database could be used at a dosage well below the dosage at which it is immunosuppressive. However, no company is likely to test a generic drug in Alzheimer's. Further, Medivation has not published details from the more sensitive assays. Regardless of the details, there are several key problems with the mitochondrial preservation theory.

With cyclosporin 100 times more potent than Dimebon in an *in vitro* assay, perhaps it has a similar advantage in humans. Fortunately, that "clinical trial" has already been completed in that the kidney transplant registry tracks clinical events in all transplant patients. In the 25 plus years that cyclosporin has been used in these patients, there has been no evidence of a lower incidence of Alzheimer's in this population. Further, renal transplant patients suffer an almost four-fold increase in melanoma. If there was a prophylactic effect of cyclosporin on Alzheimer's in this setting, it would have been observed. Second, rigorous pharmacodynamic -- what the drug does to the body -- and pharmacokinetic -- what the body does to the drug -- studies for Dimebon are not readily available. Still, it is safe to assume that Dimebon exhibits a relatively short half-life since it is dosed three times a day as an antihistamine. Therefore, if Dimebon targets the mitochondria found in virtually every cell (\approx 1,000 in a single liver cell), not much drug is going to make it to the brain. Third, Dimebon's widespread action in mitochondria should result in a broader side-effect profile than what has been observed, and is expected, from an antihistamine. Thus far, Dimebon's proposed activity in the neural mitochondria of patients with neurodegenerative diseases appears weak and far-fetched. Dimebon looks like an antihistamine and "quacks" like an antihistamine. Therefore, the simplest explanation that fits the *in vitro* data suggests that Dimebon is just an antihistamine. And maybe nothing more.

Still, the FDA does not require certainty about a mechanism of action to clear a drug. The FDA does require "...substantial evidence of effectiveness...derived from adequate and well-controlled clinical investigations."

Clinical Trials

It is important to acknowledge that data from human testing always trump pre-clinical (animal model) and *in vitro* (test tube) results. Dimebon has shown clinical efficacy in mild-to-moderate Alzheimer's from two small trials of 14 and 183 patients each. Both trials were conducted in Russia. The larger trial was initiated in September 2005 and its results were reported in The Lancet last July (Table 1). Last June, the Company initiated another trial in 525 patients. Medivation will conduct this trial in the US, Europe and South America. Finally, Medivation has also tested Dimebon in a small Phase 2 trial for Huntington's. Medivation's clinical experience with Dimebon is summarized in Table 1 and discussed in detail below.

Table 1
Clinical Trials With Dimebon

Indication	Number of Patients	Trial Location	Dimebon Source	Reference
Alzheimer's	14	One site in Russia	Russia	Ann. NY Acad. Sci., Vol. 939, pp. 425-435, 2001
Alzheimer's	183	Eleven sites in Russia	Russia	The Lancet, Vol. 372, pages 207-215, 2008
Huntington's	91	15 US and 1 UK site	US	Neurotherapeutics, Vol. 6, page 203, 2009
Alzheimer's	525	\approx 30 US and 30-50 more in Europe and S. America	US	Initiated June 2008. See www.clinicaltrials.gov, updated Jan. 23, 2009

First clinical trial: Data for fourteen Alzheimer's patients published in 2001

Four months after the issuance of the patent cited above, a publication in *Annals of the New York Academy of Sciences*, again by Bachurin et al. and again including Dr. Sablin described, among other things, the testing of Dimebon in 14 patients (13 women) with mild-moderate Alzheimer's. This appears to be the first published clinical trial of Dimebon in Alzheimer's and was predicated on *in vitro* and laboratory animal studies, some of which were also reported in this paper (Table 1).

The trial was a single-arm, single site test of Dimebon dosed orally at 20mg, three times per day for an eight-week course of therapy. The dosage is the same regimen used for Dimebon as an antihistamine. Patients were evaluated after four and eight weeks of therapy, then eight weeks after therapy was discontinued. Evaluations included the Hazegawa scale which is similar to the Mini-Mental State Exam (MMSE) used in the US for cognitive function and the Bukatina scale. The Bukatina scale was created by one of the authors and employs a 0-4 symptom score where 4 indicates the highest deterioration. According to the authors, the main objective of the trial was to assess the efficacy of Dimebon. Since the trial lacked a bona fide control arm, it appears that Dimebon's efficacy was a foregone conclusion. At the time of this publication, four Alzheimer's drugs had been FDA approved in the US and all had employed the ADAS-cog scale (Alzheimer's Disease Assessment Scale-cognition) as part of their primary clinical endpoint in pivotal trials. The ADAS-cog uses 11 measures of cognitive function resulting in a score from 0 to 70, where a high score indicates poor cognitive function. None of the four drugs had used the Hazegawa or Bukatina scales.

For a "first-in-Alzheimer's-man" test, the trial is small, of short duration, used an unconventional clinical endpoint and did not test alternative dosages or dosing regimens. While a few other drugs have demonstrated clinical utility in two, nominally unrelated indications (e.g., Merck's Proscar® dosed at 5mg, once-a-day for benign prostatic hypertrophy and, as Propecia®, dosed at 1mg, once-a-day for hair loss), dosing is usually different, based on clinical data, for each indication. The assumption that Dimebon would prove as active when used chronically in Alzheimer's at exactly the same dosage that is used occasionally, over five-to-ten day intervals, as an antihistamine is highly speculative. Further, the absence of any dose-ranging studies reflects a sub-par clinical development plan.

In addition, the paper describes as a "control" group eight Alzheimer's patients who received placebo for four weeks. Patients were not randomized to Dimebon or placebo. Still, the authors compared the two groups for changes in cognitive functions, using the Bukatina scale, after four weeks of treatment. The difference was highly significant at $p < 0.01$. Curiously, comparative data after eight weeks of treatment were not reported.

Poor clinical trial design coupled with selective reporting of inherently weak data are bad omens. Despite these flaws, the authors asserted:

"The results of the study reported here show that Dimebon has a great potential as a new medication that may not only improve cognitive functions, but, most importantly, may prevent the progression of the disease."

Second clinical trial: Data for 183 Alzheimer's patients published in 2008

Without question, excitement about Dimebon's potential in Alzheimer's currently hinges on the data from what the FDA has deemed to be a pivotal Phase 2 trial in 183 mild-to-moderate Alzheimer's patients. Briefly, this was a double-blind, placebo controlled study conducted at 11 sites in Russia. Treatment was for the commonly utilized 26 week period with an optional, blinded, 26-week extension. The first week employed, for Dimebon, a 10mg, three times a day "run-in," which is not unusual, followed by 25 weeks at 20mg, three times a day. The primary clinical endpoint was change from baseline to week 26 in the conventional ADAS-cog score in the 89 patients on Dimebon versus the 94 on placebo. The comparison employed a rigorous, intent-to-treat analysis with last observation carried forward imputation. Importantly, Dimebon was sourced from NPO Organika, a small, Siberian manufacturer founded in 1962 with 2007 revenues of \approx \$25 million. NPO Organika was also the drug supplier for the 14-patient trial described above. However, a US source manufactured the Dimebon used in both US-based trials (see Table 1) reported below. Medivation has not indicated who the source is.

There were several interim reports of data from this trial. One of the first was in a Company press release dated September 21, 2006 describing the six-month results, i.e. at the time of the primary clinical endpoint. Roughly 85 percent of the patients randomized into each arm completed the trial. Specifically, 78 patients (88%) on Dimebon and 77 (82%) on placebo completed the 26 week treatment. Simply put, the reported results were stunning. Dimebon met all five efficacy endpoints with statistical significance compared with patients on placebo. The only adverse event ("AE") of numerical significance was dry mouth which affected 12 of 89 (13.5%) patients on Dimebon. As subsequently reported in the Lancet paper, one patient in the placebo arm (1.1%) experienced dry mouth. Antihistamines typically cause dry mouth, so the effect was not surprising.

About 85 percent of the eligible patients from each arm continued in the blinded, six-month extension trial. Specifically, 68 patients (87%) on Dimebon and 66 (86%) on placebo for a total of 12 months. In its June 11, 2007 press release, Medivation reported the data from the 12-month follow-up study. Again, Dimebon met all five efficacy endpoints with statistical significance compared with patients on placebo and, the benefits of Dimebon over placebo were equal to or better than those observed after six months. Roughly 90 percent of the patients randomized into each arm completed the six-month extension trial. Specifically, 61 of 68 patients on Dimebon and 59 of 66 on placebo completed. Dry mouth continued to be the dominant AE, at 18.0 percent of the original 89 patients on Dimebon versus one patient in the placebo cohort. Somewhat more worrisome was the statistically significant difference in the serious adverse event ("SAE") rate. There were three SAE (3.4%) in the Dimebon cohort and, at 11 (11.7%), more than three times as many SAE in the placebo arm ($p=0.03$).

While the number of deaths in each arm, at each time point, were the same with one death each at six months, and two deaths each at 12 months, further details of the SAE were not described in the Lancet publication. Usually, SAE are more prevalent in the drug arm of a placebo-controlled study, so this *reversed* observation deserves greater attention than it received.

Complete study results from this pivotal Ph 2 trial were published in July 2008 (Table 1). Curiously, the most common AE in the trial was an increase in serum creatine kinase (CK), an indication of muscle damage. Although musculoskeletal pain was reported in three patients on Dimebon versus none on placebo, the increase in CK was more equally balanced between the two arms, affecting 15 patients on Dimebon (17%) and 13 patients on placebo (14%). Typically, elevated serum values are not worrisome unless they exceed three times the upper limit of normal. That was not the case and the cause for these increases remains unknown.

One potential source of bias in the trial might lie in clinical site participation. Although each site enrolled at least six patients, that is far below the average of 16-17 patients per site adequate randomization should have generated. In fact, one of the authors was the principal investigator at the highest enrolling site. A bit more transparency and critical skepticism by The Lancet's editors appears to have been called for.

Although this trial was relatively small to be pivotal, clearly it was designed as only a Phase 2 trial. Still, the reported results were so compelling that the FDA agreed to treat it as the first of two pivotal trials which, if a second is positive, will support an NDA submission for approval. Further, the data reported in The Lancet are nothing less than extremely encouraging. There are elements of "defensiveness" by the authors in the text, presumably in response to some skepticism by the paper's reviewers. For example, explicit confirmation of patient randomization, blinding and case report form quality are addressed in this paper. Most clinical research papers rarely address such routine protocol items. To quote, "Taken together, these findings suggest that the study methodology was sound." This statement alone suggests that someone thought the study's methodology might be flawed. Still, at face value as a stand-alone report, there can be no question as to Dimebon's potential to treat Alzheimer's. Unfortunately, the report does not stand alone.

The history of Dimebon and the lack of routine pharmacologic investigation raise disturbing questions about the scientific rationale supporting the initiation of this study. And, a subsequent, US-based clinical trial with Dimebon raises even more questions.

Third clinical trial: Data for 91 Huntington's patients reported in 2009

Unlike Alzheimer's, in which cognitive function such as memory decays, patients with Huntington's (also called Huntington's *chorea*) exhibit involuntary, spasmodic movements of the limbs and facial muscles. It is inherited as a single gene defect causing progressive physical, and some mental deterioration.

Begun in July 2007, this Phase 2 trial was a double blind, placebo controlled study of Dimebon dosed as always in patients with mild-to-moderate Huntington's treated for a 90-day course of therapy. Enrollment was at one UK and 15 US sites and Dimebon was sourced from a US manufacturer. Thus, this study was both the first trial of US-sourced Dimebon and the first trial conducted outside of Russia. Ninety-one patients were randomized 1:1, with 46 patients on Dimebon of which six dropped out and 45 on placebo where eight dropped out. The primary endpoint was the ability of patients to complete 90 days of therapy on Dimebon, described as safety and tolerability.

Secondary endpoints included UHDRS which is the gold standard Unified Huntington's Disease Rating Scale plus ADAS-cog and MMSE scores, neither of which are routinely used in Huntington's trials. The UHDRS measures motor function from zero to four where zero is no involuntary movements, at seven body sites resulting in a score from 0 to 28. A high score indicates increasing disease severity. Top line results were reported last July 7, followed by an abstract published in January 2009 (Table 1).

While the drug was well-tolerated, of course, it did not demonstrate efficacy by UHDRS. The Company press release did highlight the statistically significant ($p=0.03$) improvement in cognition, based on the MMSE score, though there was no improvement based on ADAS-cog. Medivation also highlighted the fact that patients on Dimebon had fewer falls (9%, four patients) than on placebo (16%, seven patients). These are good things.

However, unlike patients in the Alzheimer's trial where dry mouth was a common side effect of Dimebon affecting 14%-18%, only two patients (4%) had dry mouth versus three (7%) on placebo. Further, in this trial, the most common problem was headache, affecting eight or nine (19%) patients on Dimebon versus three (7%) on placebo. Headache was not even mentioned in the Lancet paper. Something looks wrong.

Although different patient populations might respond very differently to the same drug, a simpler explanation might be that this Dimebon which was manufactured in the US is different from the Dimebon manufactured in Russia. Other explanations for the discrepancy are also possible. It's difficult to know the cause with certainty, but discordant adverse event profiles like headache and dry mouth, especially for an antihistamine, raise questions.

Finally on this topic, Medivation's July press release is telling. The Company highlights the positive MMSE result and the significantly fewer SAE, e.g., fewer falls, while apparently missing/ignoring the difference in dry mouth incidence from that observed in the Alzheimer's trial. When Dr. Hung was asked about the dry mouth difference, he described this trial as too small for comparison. When a company portrays a trial as large enough to accentuate the positive, especially endpoints of no regulatory value, yet too small to acknowledge the negative, investors should be wary.

Phase 3 Clinical Trial

Last June, Medivation initiated a second pivotal trial to test Dimebon for efficacy in mild-to-moderate Alzheimer's patients. Called The Connection Study, this double blind, placebo-controlled trial plans to enroll 525 patients into three arms including Dimebon at 5- and 20mg, each three times per day or placebo for a 26-week course of therapy. Enrollment was planned for up to 100 sites comprising 30 in the US with the others in Europe and South America. In August the plan was scaled back to 60-80 sites. In fact, as of early September, 27 US sites were enrolling patients and, as of late January 2009 (Table 1), 27 US sites were recruiting and another was active, though not recruiting. The co-primary endpoints are ADAS-cog and CIBIC-plus which is a measure of global function including input from caregivers. Every element of this trial is conventional and reflects a solid clinical development plan.

Initially, final data were to be reported in July 2010, but after partnering with Pfizer (see below), an NDA submission to the FDA may be delayed until 2011. Apparently and reasonably, Pfizer wants to study Dimebon in patients with more advanced Alzheimer's, so-called moderate-to-severe disease, in combination with other drugs approved to treat Alzheimer's such as Pfizer's Aricept and for up to 12 months of therapy, rather than six. It is worth noting that the key Dimebon use patent cited on the first page expires in October 2016.

Pfizer Likes Dimebon

In early September 2008, Pfizer inked a \$725 million deal with Medivation for world-wide rights to Dimebon, paying \$225 million up-front. Pfizer picks up 60 percent of the costs and gets 60% of the profits. Thus, more than half the cost burden of the Phase 3 trial is now borne by Pfizer. Also in September, Pfizer announced that it was exiting several disease areas, including anemia, hyperlipidemia and obesity among others. Priority would be given to Alzheimer's disease, diabetes and oncology, among others. In addition, Pfizer sells Aricept, the second drug approved by the FDA to treat mild-to-moderate Alzheimer's and a current blockbuster with worldwide sales in 2008 of \approx \$1.6 billion. However, Aricept's key patent expires in November 2010. Clearly, finding a new Alzheimer's drug, such as Dimebon, makes sense for Pfizer.

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Investment Risks (support for a short thesis)

- The original premise behind testing the antihistamine Dimebon in Alzheimer's relied on its declared activity as an acetylcholinesterase inhibitor (like the first four FDA approved drugs) and as an NMDA inhibitor, like Namenda. Positive results were reported for 14 patients with Alzheimer's. Within a few years, a new theory for Dimebon's activity, one of ameliorating mitochondrial dysfunction, was proposed. Flawed theories have led others to unexpected success, but such flukes are rare. Two theories dominate the Alzheimer's world and a new theory looks like a dodge to distract from an originally weak thesis.
- Dose-ranging and alternative dose regimen studies have not been reported. Chronic usage (for Alzheimer's) is very different from the five to ten days common to antihistamine use.
- The 14-patient trial in Russia was too small, too short, lacked a control arm and employed an unconventional clinical measure of success. Expressions of success ("great potential") by the authors were unwarranted.
- The 183-patient trial published in The Lancet appears extremely compelling. However, the risk of site bias leading to grossly unequal randomization of patients is a concern. The increase in creatine kinase, even if relatively balanced across both arms, is a second concern. The absence of details regarding the three-fold difference in serious adverse events (placebo > Dimebon) is a third concern.
- Discordance in the adverse event profile of Huntington's versus Alzheimer's patients tested with Dimebon is worrisome. Perhaps antihistamines do not cause dry mouth in Huntington's patients or perhaps Dimebon manufactured in the US differs from that manufactured in Russia. Relatively benign adverse events like dry mouth and headache can serve as internal controls in a clinical trial. As such, these controls are not congruent and lack harmony.

The elephant in the room

Finally, there are really only two explanations for the remarkably positive Phase 2 data reported for Dimebon in the Lancet paper. The first is that despite several flawed or unsubstantiated hypotheses (dosing, mechanism of action) Dimebon is truly a superb treatment for Alzheimer's. To borrow a quote by Louis Pasteur, "Chance favors the prepared mind." In which case, Medivation's founders and associated researchers are to be commended for their outstanding insight. The second explanation for these data invokes fraud. By whom and to what end are not known. To borrow another quote, "You can't fool Mother Nature." The Phase 3 results, expected in less than two years, should resolve this dilemma.

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Investment Merits (support for a long thesis)

- The Phase 2 data published in The Lancet are stunningly positive. If these results bear out in the on-going Phase 3 trial, Medivation and Pfizer will have a blockbuster. However, publication in a well-respected, world-class journal is no guarantee of legitimacy. In May 2005, Woo Suk Hwang and colleagues published data in Science claiming the first human clone. By January 2006, Dr. Hwang admitted to fabricating the data for all eleven of his clones. Ultimately, all scientific enterprise depends on telling the truth. Publishing novel observations in a professional journal, even if vetted under peer review, serves only to *announce* data in need of *confirmation*. This is why fraud in science is rare. If what has been reported is novel and important, yet false, it will be found out.
- Many will view Pfizer's September investment as validation enough for an investment in Medivation. And, most young biotech companies would be ecstatic to receive \$225 million, more than 30 percent of the deal's \$725 million value, up-front. However, Pfizer's pockets are deep and \$225 million represents about 41 hours of Pfizer's 2008 revenues. Still, Pfizer may choose to acquire Medivation outright. Clearly, either positive clinical trial results or an acquisition could drive Medivation's stock up at least two-to-four fold from where it is today.