Opko Health: The Placebo Effect

Lakewood Capital Management

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/pla•ce•bo ef•fect/ (plah-se’bo ĕ-fekt’), noun [L.]:

1. the beneficial effect that occurs following a treatment administered to a group that arises simply from that group’s faith or preconceptions that the treatment will work.
2. an ineffectual treatment intended to deceive the recipient.
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OPKO HEALTH: THE PLACEBO EFFECT

The view expressed below is the opinion of Lakewood Capital Management. Lakewood currently has a short position in the security discussed herein. Lakewood may change its view or position at any time. Please do your own research.

“Oh what a tangled web we weave, when first we practice to deceive.”

– Sir Walter Scott

A.) Executive Summary

We will show below why we believe Opko shareholders have unknowingly been fed a placebo and why we believe the shares are worth 75% to 100% less than where they are currently trading. Opko is a development stage pharmaceutical company that was formed in 2007 via a reverse merger engineered by the acclaimed Dr. Phillip Frost (Chairman of Teva Pharmaceuticals and investment bank Ladenburg Thalmann). We believe shares in Opko Health (OPK) (“Opko” or the “Company”) are grossly overvalued, and at a $5 billion fully-diluted market capitalization, the shares are as disconnected from reality as any company we have ever seen.

The Company’s $5 billion fully-diluted market capitalization completely ignores:

- the Company’s history of failures, disappointments and overhyped opportunities;
- the low likelihood of meaningful commercial success in any of the Company’s products as well as the associated limitations and risks;
- the Company’s dismal financial performance;
- unrealistically bullish and perennially incorrect analyst forecasts from related and biased parties;
- concerning affiliations between the Company’s management and what we believe are serial stock promoters; and
- a cult-like following in the stock largely based on regular insider purchases that we believe are a red herring to drum up retail investor buying.

We make the following assertions:

1. **Opko has a history of overpromising and under-delivering: nearly every legacy opportunity Opko has pursued over its history has ended in delay or failure despite much initial hype.** As shown below, since its formation until the end of 2012, we have found 30 products or investments that Opko has claimed to be working on and 25 of those appear to have ended in delay, disappointment or total failure. Only 5 relatively
minor products appear to be on track. Opko has engaged in so many highly touted random deals and acquisitions that it must be nearly impossible for shareholders to even know what they own any more. Seemingly every year, the Company comes up with a brand new product or drug opportunity to capture investors’ interest and keep the story going.

2. The Company’s Latin American drug distribution business is practically worthless to Opko shareholders. Opko acquired two Latin American generic drug distribution companies for $20 million ($0.04 per Opko share), forming the basis for this business. Although it has historically accounted for the majority of Opko’s revenues, it is tiny and appears to be challenged, with an annualized gross profit of only around $10 million. After a reasonable allocation of SG&A, it is unlikely this business even makes a profit.

3. The Company’s Alzheimer’s Test (licensed for no upfront payment in 2009), which was nearly the entire basis for the Company’s value one year ago, isn’t working as hoped and is highly unlikely to ever be commercialized. This test essentially was the source of all investor interest in Opko in 2012 with the analyst at Ladenburg Thalmann predicting a market opportunity that could “approach $3 billion annually.” A license to the test was acquired for what appears to have been essentially no upfront consideration from the University of Texas-Southwestern in 2009. The basic idea was a blood test that could diagnose Alzheimer’s (currently the only definitive diagnosis is autopsy). As it turns out, the Alzheimer’s test has not proven to be as good as the initial study (which was based on just six Alzheimer’s patients in advanced stages of the disease). Today, Opko appears to have moved on, downplaying the test’s significance and making just a brief mention of it at the back of recent investor presentations. The Jefferies analyst had assigned $3 per share ($1 billion at the time) to this business just last year. Today, it has been removed from her net asset value calculations given the test’s apparent failure.

4. Claros Diagnostics (acquired for $30 million in 2011), which was repeatedly hyped by the Company, makes one product and it doesn’t work. The basic concept was to have a small blood test system that can be used to run tests in-house during a visit to the doctor without having to wait for results from a lab. There are considerable challenges to broad adoption for this system. Our research has indicated that a lot of doctors do not want to deal with the paperwork associated with in-house lab testing. Also, as one doctor

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1 Mexico operations acquired in February 2010 for $3.5mm ($1.5mm cash and $2mm stock); Chile operations acquired in October 2009 for $16mm cash (see pages 60-61 of 2010 10-K)
2 Estimated 2012 gross profit for “core” business of $10.4mm based on total Opko 2012 gross profit of $19.2mm less $3.4mm contribution from Farmadiet acquisition less $5.4mm contribution from FineTech acquisition (see pages 56 and 68 of 2012 10-K)
3 See Ladenburg Thalmann initiation report dated July 14, 2011 (page 2)
4 See Jefferies report dated August 10, 2012 (page 1)
5 Jefferies report dated August 10, 2012 assigned “~$3/sh for AD/cancers Dx” but next report on October 29, 2012 assigned no value for Alzheimer’s test
told us, “the reimbursement needs to be more lucrative to spend 10 minutes on lab work vs. 10 minutes with another patient.”

The timeline for commercialization has been repeatedly delayed from “end of year 2012” to “2013” to “2014” and now as late as “Q3 2015.” According to our discussions with the Company and a physician closely tracking the progress of Claros, the product isn’t working as it has a high failure rate. Even if they could fix the problems, one physician tracking Claros did not see a huge market opportunity, estimating the probability Claros ultimately gets to $20 million in sales at around 50% with “maybe a 5% chance they could get to $100 million in sales.” He also thought that if it were “a big market opportunity, people would have jumped on this a long time ago.” It is now rather clear to us how Opko acquired this technology for just $30 million in a competitive auction. Even if they managed to one day get the machine working, it is hard to see how it would have material value in the context of a $5 billion market capitalization company.

5. Opko’s 4Kscore™ exploratory prostate cancer screening test (licensed for no upfront payment in 2012) has serious issues, has seen numerous delays and is unlikely to amount to much revenue. In January 2012, Opko acquired a license to an exploratory prostate cancer screening test called 4Kscore™ from a small group out of Finland called Arctic Partners for no upfront payment. The basis for excitement in this test was data presented in a journal by individuals associated with Arctic Partners showing the test’s ability to reduce unnecessary biopsies. However, an accompanying editorial in the same issue raised serious questions around the value of such a test, pointing out that “…24% of all cancers and 14% of high-grade cancers would be missed.” The test has been significantly delayed and after a 2012 launch in the U.K. and promises of a 2013 launch in the U.S., the test has not produced any material revenues. Furthermore, Opko is planning to launch the test out of a small lab it acquired in the U.S. with a tiny sales force and any patients using the test will likely have to pay out of pocket given insurance reimbursement issues.

6. Rayaldy (aka CTAP101), the lead candidate of Cytochroma (acquired for $100 million in stock in 2013), faces serious obstacles and is unlikely to generate enough sales to result in material value for Opko shareholders. Rayaldy is targeting patients with secondary hyperparathyroidism (SHPT) in Stages 3 and 4 of chronic kidney disease (CKD). Patients are currently treated with over-the-counter vitamin D which can cost

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6 Based on discussions with a neurologist on November 15, 2011
7 Per discussions with the Company at Lazard conference (November 15, 2011)
8 See page 7 of 2011 10-K
9 See page 7 of 2012 10-K
10 See slide 26 of September 2013 investor presentation
11 Per discussions with the Company at Jefferies conference (June 4, 2013)
12 Per discussions on November 7, 2013
just $5 per bottle or vitamin D analogs like Hectorol and Zemplar that both go generic next year and will likely see their price plummet.

We have spoken with numerous nephrologists who treat patients with SHPT and the tone was skeptical. For example, Dr. Jeffrey Giullian, a veteran nephrologist who has about 500 CKD patients in his clinic, had the following to say when we discussed Rayaldy (CTAP101) and its market potential with him:

“In Stage 3 and 4 chronic kidney disease, you don’t really see the side effects of giving OTC vitamin D ... there’s the rub ... you can give OTC or calciferol without the side effects. It’s later when the kidney is struggling that the nutritional vitamin D causes the side effects, but at that point we’re switching over to the analogs [such as Zemplar or Hectorol]. So it’s hard for me to see a niche for CTAP101 ... in early stages of treatment you can use nutritional vitamin D and in later stages you want to use Zemplar or Hectorol... I would think they [Cytochroma] are overstating the market opportunity... I have probably 500 [CKD] patients in my clinic ... maybe 4 or 5 of them could benefit from switching to CTAP101. The issue is this is a new drug that is just barely better than existing treatments that are over-the-counter and cheap. So would it justify a huge difference in cost, probably not.”

Even the bullish Jefferies analyst concluded after speaking with nephrologists there was not a “significant unmet need” in treating SHPT patients:

“Nephrologists note that for vitamin D insufficiency, patients with SHPT can easily take OTC vitamin D supplements, along with generic vitamin D analog, rather than paying a premium for new vitamin D analogs.”

We believe Rayaldy is worth at most $500 million or just $1 per Opko share, and at this aggressive valuation, it would represent a value of five times what Opko paid to acquire Cytochroma just a few months ago.

7. Proior Biotech’s (acquired in 2013 for $480 million in stock) lead drug candidate will likely be beaten to market by LG Life Sciences and its own financial advisors valued the company below Opko’s purchase price. In April 2013, Opko announced the acquisition of a Frost-backed public company called Proior Biotech (“Proior”) for $480 million in stock. Proior’s lead product is a Phase 3 long-acting human growth hormone. Unfortunately for Opko, Proior has been beaten to the punch by LG Life Sciences, who will likely have a nearly identical drug on the market next year, before Proior even hopes to complete its studies. A read of the merger proxy reveals that

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13 Per discussion on November 6, 2013
14 See Jefferies note from March 19, 2013 (page 3)
15 Oppenheimer valued Proior at $3.32-4.23 per share (~40-53% discount to Opko’s $7.00 per share purchase price); see page 69 of OPK/PBTH merger proxy for Oppenheimer valuation analysis
another company (likely Teva) passed on an acquisition of Prolor after conducting due diligence. Furthermore, the proxy shows that Prolor’s own financial advisors valued the company at roughly half of Opko’s purchase price and valued the lead Phase 3 drug at only $131 million to $174 million, or just 2.6% to 3.4% of Opko’s current fully-diluted market capitalization.

8. Opko’s CEO, Dr. Phillip Frost, has a history of close financial ties with what we believe are two serial stock promoters, who have both been the subject of several lawsuits, and the Company’s former CFO curiously was the Treasurer of a Frost-backed penny stock (while he was CFO at Opko), which went on to merge with a Chinese company that turned out to be a fraud. While Dr. Frost has earned the admiration of the investment community after selling two companies (Key Pharmaceuticals and Ivax Corporation) for incredibly large gains, we think there is another side of his career that should be of great concern anyone investing in Opko. Dr. Frost has a disturbingly large number of connections to what we believe are two serial stock promoters that have each been the subject of multiple lawsuits, Barry Honig and Michael Brauser (who together run an entity called Marlin Capital). We have counted 16 different penny stocks in which Frost, Honig and Brauser have invested together in recent years, including entities in which Opko is directly involved. In fact, the business address listed for Honig and Brauser, 4400 Biscayne Blvd., is owned by Dr. Frost and is also the offices of Opko Health, Ladenburg Thalmann (where Dr. Frost is Chairman) and numerous other companies in which Frost, Honig and/or Brauser are involved (including MusclePharm, BioZone, SafeStitch Medical, Non-Invasive Monitoring Systems and others). In fact, Barry Honig’s office is listed as being in the exact same suite (Suite 850) of 4400 Biscayne Blvd. as Dr. Frost’s Frost Gamma Investments Trust.

Dr. Frost has also been involved in plenty of other penny stocks beyond those with any apparent Honig or Brauser involvement. Perhaps the most remarkable situation is that of Protalix BioTherapeutics (PLX), which was merged with Orthodontix (traded on the pink sheets under OTIX) in August 2006. Simultaneously, Frost and Glenn Halpryn (who together owned a majority of Orthodontix) agreed to invest $15 million in Protalix. At that time, Frost and his trusted lieutenant, Dr. Jane Hsiao (who is the current Vice Chairman and Chief Technical Officer of Opko) joined the Protalix board. Interestingly, Eli Hurvitz was the Chairman of Protalix at the time and was also the Chairman of Teva at that point. Amazingly, on October 24, 2007, Protalix announced a 10 million share offering at $5 per share vs. the prior close of $36.06 per share, an astounding 86% discount. The next day, the stock fell 83%, “wiping away $2.07 billion in market value.”

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16 See OPK/PBTH merger proxy (page 49)
17 See OPK/PBTH merger proxy (page 69)
18 See Document Security Systems (DSS) filing (page 169)
Dr. Frost and Hsiao, who had joined the board on 12/31/06, quit the Protalix board after the company’s implosion, with the press release citing “personal reasons.”

If all of this is not concerning enough, consider the following facts related to Opko’s former CFO. On July 16, 2012, long-time Frost colleague Rao Uppaluri retired from his role as CFO of Opko and was replaced by Juan Rodriguez. We find it strange that Uppaluri was listed as Treasurer and Director of Ideation Acquisition Corp, a publicly-traded company, as recently as a 10-K filed on March 20, 2009 when at that same time, he was the CFO of Opko.19 But, Uppaluri’s bio in the Opko 10-K filed around the same time only discloses that he was on the board of Ideation (not that he was Treasurer).20 Also, Dr. Frost served as the Chairman of the Board for Ideation at that time. Ideation ultimately merged with a company in China, changing its name to SearchMedia. SearchMedia was ultimately discovered to be a fraud, with its auditor KPMG resigning from the account.

9. The only significant sell-side Opko research coverage comes from Ladenburg Thalmann (Dr. Frost’s company) and Jefferies (the Company’s lead underwriter and M&A advisor), both of which have repeatedly been way too aggressive. Ladenburg’s initiation report in 2011 claimed the market opportunity for Opko’s Alzheimer’s test “could approach $3 billion annually.”21 We now know this test appears to be a failure. The same analyst projected Opko will be cash flow positive in 2014 and may not need additional capital (of course, Opko losses have mounted since and the Company has already raised capital through convertible notes).

The Jefferies analyst valued Claros at $1 billion in her price target calculation despite Opko having just bought Claros a month earlier for $30 million in a competitive auction.22 Even after acknowledging delays in key programs (including the Alzheimer’s test which she said could generate more than $800 million in sales), she did not make any changes to her price target (upping the value of other projects to make up the difference). In subsequent reports, she pointed out delays in 4Kscore™ and Claros, yet she actually increased her price target.

10. Opko’s CEO regularly purchases shares in Opko (which is commonly stated as the predominant reason to buy the stock), but we believe this is a red herring. Dr. Frost has consistently purchased Opko shares in the open market and many investors seem to be buying the stock at any price based on this fact alone. The logic seems to go, “if Phil is buying, surely he must know something.” Investors have been trained to follow insider buying, and we believe Dr. Frost has likely taken advantage of that fact to draw in

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19 See Ideation 10-K (page 41)
20 See Opko 10-K (page 21)
21 See Ladenburg Thalmann initiation report dated July 14, 2011 (page 2)
22 See Jefferies initiation report dated November 10, 2011 (page 1)
unsuspecting retail buyers who don’t fully understand what they own. We imagine Dr. Frost at this point realizes he is effectively “pot committed” in Opko, and if he stops buying shares in the open market, confidence would likely disappear and the stock could plummet (his stake is also worth an astonishing $1.9 billion, which is a lot for anyone to fight hard to hold on to… not to mention what must be a keen interest in maintaining the support and trust of his followers). 23

Consider this: Frost has engaged in insider purchases at Opko for years going back to 2007, and it is rather obvious now in hindsight that he didn’t “know something” after all, since nearly everything the Company was working on throughout that period has been a failure or disappointment (the Company’s main assets today were mostly acquired just in the past year). Perhaps even more importantly, shareholders might want to consider that for every share that Dr. Frost has purchased in the open market, the Company has issued nearly six more to finance acquisitions and raise capital over the years (fully-diluted shares have increased from 201 million in 2007 to 470 million today) – not the behavior we would expect from a company that believes its shares are a good value.

11. After years of shareholder dilution, Opko’s market capitalization has swelled to $5 billion despite all of the above issues. Opko’s fully-diluted share count has expanded from 201 million fully-diluted shares immediately following the Company’s formation in 2007 to 470 million fully-diluted shares (the calculation is provided later in this report). As Opko’s share price has increased from around $4 per share two years ago to over $11 per share today, the Company’s market capitalization has soared from under $1 billion to $5 billion in just two years.

We draw the following conclusions from the foregoing assertions:

1. With a run-rate operating loss now exceeding $100 million annually (with Prolor Biotech losses included), we believe it is unlikely shareholders will ever see a profit out of Opko. For six straight years, Opko has lost money despite having worked on over twenty projects that were supposed to deliver financial results over that time frame. In recent years, the losses have increased sharply as the Company has continued to ratchet up its acquisition efforts. The realistic revenue opportunities of Opko (please see our individual discussions on each product) are unlikely to cover its ever-mounting losses.

2. We believe the shares are worth 75% to 100% less than where they are currently trading. It is our belief that Opko will never report a profit, which would render an ultimate price for the stock of $0 per share. Even under an incredibly optimistic scenario whereby the 4Kscore™, Cytochroma and Prolor Biotech were each worth $500 million

23 Based on an estimated 172.8mm diluted shares beneficially owned by Frost, The Frost Group, LLC and Frost Gamma Investments Trust, pro forma for the Prolor acquisition and including all warrants, options and convertible debt based on the treasury method; based on latest 13D plus subsequent open market share purchases
and all other assets generated enough money to cover operating losses (thereby netting to a value of zero), the stock would only be worth $3 per share, or nearly 75% below the current price.

3. **We believe Opko’s stock has become little more than a day trading vehicle.** Opko’s stock has over 100 message board postings on Yahoo! Finance daily… that is five times more than Johnson & Johnson, Pfizer, Merck and Eli Lily combined. The stock is frequently cited on CNBC’s *Mad Money* (which is widely watched by retail investors) and there have been 32 positive write-ups posted on Seeking Alpha in 2013 alone. No institution owns more than 3% of the stock and the largest institutional shareholders (Vanguard and Blackrock) appear to be index funds. Our experience with stocks possessing these characteristics indicates they are very fragile and quite frequently expose shareholders to large, sudden price declines.

4. **Opko’s float has expanded considerably in recent months, making it less likely that the shares will be artificially inflated in the future.** We estimate the free float of Opko has expanded from $650 million one year ago to $2.5 billion today due to (1) the all-stock acquisitions of Cytochroma, Prost-Data and Prolor Biotech, (2) the partial early conversion of convertible debt into equity and (3) the sharp rise in the share price. Furthermore, the stock has been **added to the TASE 25 index** (Tel Aviv) and saw its weighting in the Russell 2000 increase at the end of August, which in turn have increased the shares that are available for borrow (as index funds generally lend out their shares). As a result, Opko shares can now be borrowed by short sellers at a current annual rate of <10% whereas they were nearly impossible to borrow over the course of the past year. Historically, Opko’s stock was fairly easy to impact with insider share purchases and retail investor influence given its tiny float. We believe Dr. Frost’s buying combined with intense retail buying and unrealistically bullish analyst research had an outsized impact on Opko’s stock price historically, but now with the current free float having more than tripled in value over the past year, we believe it is much more likely that Opko’s shares will reflect reality in the future.

**B.) A Dizzying History Of Deals And Disappointment: Other Than Stock Promotion, We Can’t Find Much Opko Has Done Well**

As shown below, since its formation until the end of 2012, we have found **30** products or investments that Opko has claimed to be working on and **25** of those appear to have ended in delay, disappointment or total failure. Only 5 relatively minor products appear to be on track. Opko has engaged in so many random deals and acquisitions that it must be nearly impossible for shareholders to even know what they own any more.
Below is a year-by-year account of all the deals in which Opko has been involved (to our knowledge). In nearly every case, the opportunity initially sounded exciting, but the vast majority ended in utter disappointment. Astonishingly, nearly all of the recent investor excitement seems directed at assets that were only acquired in the last year for a fairly modest sum... $5 billion of market capitalization for a company that produced nothing for five years and then made a few relatively minor deals in late 2012 and 2013.

2007

Opko was formed in 2007 via a reverse merger engineered by Dr. Phillip Frost (Chairman of Teva Pharmaceuticals and investment bank Ladenburg Thalmann) involving three companies called Foptix, Acuity and eXegenics. Foptix and Acuity were both working on certain treatments for eye disease and eXegenics was a public shell with no operations. On June 8, 2007, the Company changed its name to Opko Health. From the time of the merger until 2009,
Opko was focused on the eye market, pursuing more than ten different compounds, none of which met with any success. In the spring of 2007, Opko acquired a 33% stake in a company called Ophthalmic Technologies (OTI) for $5 million in cash. In November, they acquired the remaining 67% for $10 million in stock.\(^{24}\) Four years later, in September 2011, Opko would ultimately sell the business for $17.5 million.

In December 2007, the Frost Group (controlled by Dr. Frost) invested $20 million into Opko’s stock at a 40% discount to the 5-day average share price. “We are pleased to make this investment during this important Phase of Opko’s product development efforts, with our lead drug candidate bevasiranib in Phase III trials and the recent launch of our breakthrough diagnostic imaging system,” Dr. Frost said at the time. Those important product development efforts ultimately resulted in the complete failure of bevasiranib with Opko’s decision to terminate the Phase III trial in March 2009.

In addition to the products discussed above, at the time of its 2007 10-K, Opko was working on numerous other products. Here is a list of those products and where each one currently stands:\(^{25}\)

- **Civamide, a phase I/II treatment for dry eye** → Never commercialized; last mentioned by the Company in an investor presentation in November 2009
- **ACU-HHY-011, a pre-clinical treatment for Wet AMD and Diabetic Retinopathy/DME** → Not mentioned again after the 2009 10-K
- **ACU-XSP-001, a pre-clinical treatment for Allergy and Inflammation** → Not mentioned again after the 2008 10-K
- **Wound Dressing, late-stage research for post-surgical wound healing** → Not mentioned again after the 2008 10-K
- **ACU-HTR-028, a pre-clinical wound-healing-Antifrobtic** → Not mentioned again after the 2008 10-K
- **Dry-AMD compound, a pre-clinical treatment for AMD** → Not mentioned again after the 2009 10-K

2008

In February 2008, Opko and a now-defunct penny stock named Pathogenics (PTGN) announced the publication of preclinical data demonstrating the potential utility of their formulation for the treatment of Acanthamoeba keratitis, a serious eye infection. After this press release and the 2007 10-K filed in March 2008, Opko never mentions this treatment again. In fact, the 8-K filed

\(^{24}\) See Opko 2007 10-K (page 56-57)
\(^{25}\) See Opko 2007 10-K (page 7)
in February 2008 for this press release was the last SEC filing ever made by Pathogenics and the company's website doesn't even appear to exist anymore.

In March 2008, Opko announced it had received a warning letter from the FDA finding deficiencies in record-keeping and reporting systems for OTI (which it acquired in 2007). In May 2008, Opko acquired a company called Vidus Ocular for $1.3 million in stock that was developing a glaucoma drainage device called Aquashunt. A clinical trial began in January 2009 but nothing appears to have ever come of it. In June 2008, Opko acquired a license to a “novel” small molecule for the treatment of viral conjunctivitis called Doxovir (subsequently, this product has not been mentioned in any SEC filing since mid-2010). In August 2008, Frost Group made a $15 million investment in Opko, again at a 40% discount to the 5-day average share price. In October 2008, Opko acquired exclusive rights for the treatments of allergic conditions of the eye called Budesonide. That drug was not even mentioned in a single SEC filing after the 2008 10-K and appears to have quietly failed to make any progress.

In addition to the previously discussed opportunities, at the time of its 2008 10-K, Opko was working on two additional products. Here is the list and where each currently stands:

- **OPK-HVB-004, a pre-clinical treatment for wet AMD/DR/DME** → Not mentioned again after the 2009 10-K
- **OPK-HVB-010, a pre-clinical treatment for wet AMD/DR/DME** → Not mentioned again after the 2009 10-K

2009

In March 2009, the Company’s main product, bevasiranib (a treatment for macular degeneration), failed to reach feasibility and Opko’s stock fell to just $0.60 and its market capitalization fell from a peak of roughly $600 million down to a low of $200 million.27 In June 2009, Opko completed a private placement at $1 per share (prior close was $1.20 per share). None of the original main eye treatments were ever to be heard from again.

Opko then shifted strategies and began acquiring a large number of early stage medical companies. In June 2009, Opko invested in a private company called Sorrento Therapeutics (SRNE) with a technology for the generation of fully human monoclonal antibodies. "The therapeutic antibody market is experiencing a significant growth phase and is one of the fastest growing pharmaceutical market segments," said Dr. Frost at the time. "Opko is pleased to secure a stake in this cutting edge company.” After the Opko investment, the thinly-traded Sorrento saw its stock rise as high as $75 per share in April of 2010 before crashing back down to its current price below $9 per share (with Opko selling shares regularly since August 2013). In June 2009, Opko invested in a company called Cocrystal Discovery that was focused on antiviral

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26 See Opko 2008 10-K (page 8)
27 Opko closing share price on March 11, 2009
Cocrystal… is moving quickly to fill an important void in the therapeutic armamentarium," said Dr. Frost at the time. "Opko is pleased to work with Cocrystal's world-class scientific team to create a new key player in the world of pharmaceuticals." In the more than four years since Opko made its investment, there has been little apparent progress at Cocrystal as disclosed by Opko and the book value of the investment is just $2.5 million.\(^{28}\)

In **June 2009**, Opko acquired a license for a new platform that could possibly be used to diagnose Alzheimer’s disease. This became the Company’s lead asset in 2011 and 2012 and is discussed in detail later below. In **July 2009**, Opko entered into a license with Academia Sinica in Taipei to develop proteins against influenza. "The entire Opko team is excited to be working with Academia Sinica and Dr. Wong to develop products which deal with important unmet medical needs," said Phillip Frost, M.D., Chairman and Chief Executive Officer of Opko. "Academia Sinica has long enjoyed a reputation for being the most prestigious academic institution in Taiwan and we, at Opko, are honored to have been selected to help translate the fruits of its scientific work into products to prevent and treat serious medical problems," said Dr. Frost at the time. In the more than four years since this announcement, there has been no apparent progress on this program.

In **October 2009**, Opko acquired a Chilean pharmaceutical distribution company for $16 million in cash. In **October 2009**, Opko acquired a compound from Schering-Plough called Rolapitant. The product was subsequently sold to Tesaro (TSRO) in December 2010 for an upfront payment of $6 million (plus milestones and royalties).\(^{29}\) Phase 3 data for Rolapitant is scheduled to be released soon. However, Rolapitant would face other competing treatments and our discussions with physicians indicate that there might not be a need for this product.

The 2009 Opko 10-K also mentioned a treatment for chronic cough called SCH 900978 that was in Phase II development.\(^{30}\) After not being mentioned by Opko since a June 2011 investor presentation, the product has suddenly re-emerged in Opko’s **June 2013 investor presentation** as part of its clinical pipeline with indications for not only chronic cough, but overactive bladder and major depression too (but then was once again removed in Opko’s **September 2013 investor presentation**).

**2010**

In **February 2010**, Opko acquired a Mexican pharmaceutical distribution company and announced a collaboration with a Mexican research center to develop vaccines for flu, dengue fever and West Nile virus (there has been no further mention of these efforts for the past 2.5 years). In **November 2010**, Opko invested in an antibody drug discovery biotech company called Fabrus LLC. “Fabrus is using its proprietary antibody screening and engineering approach to

\(^{28}\) See Opko 9/30/13 10-Q (page 20)  
\(^{29}\) See Opko 2010 10-K (page 10)  
\(^{30}\) See Opko 2009 10-K (page 9)
discover promising lead compounds against several important oncology targets,” said Dr. Frost at the time. “We believe the Fabrus discovery approach is novel, rapid, provides valuable data at very early discovery stages, and can screen multiple targets or pathways in parallel. We are pleased to secure a stake in this cutting edge company, and we look forward to rapidly developing important drug candidates.” It has now been three years and Fabrus does not appear to have “rapidly” developed anything and the carrying value of Opko’s investment equals just $650,000.31

2011

In January 2011, Opko announced it was collaborating with Bristol Myers Squibb on its blood test for Alzheimer’s. In Opko’s 2011 10-K, it described the Alzheimer’s test as its “most advanced molecular diagnostic test” for its “lead program.”32 While we will later discuss in detail the history of this test, this program about which the Company was most excited has been a complete failure and is barely even discussed today. Then, in February 2011, Opko acquired a company called CURNA for $11 million that was working on the discovery of new drugs for a variety of illnesses.33 “Opko is pleased to acquire CURNA,” said Dr. Frost at the time. "We believe CURNA's unique technology may be important for treating diseases in which increased levels of specific proteins are important, such as APOA1 to increase HDL levels to prevent heart disease, and genetic disorders in which higher levels of specific enzymes or other proteins may be beneficial or curative.” This acquisition appears to be making limited progress, with Opko’s most recent investor presentation describing its AntagoNAT platform as “preclinical.”

In March 2011, Opko completed a public offering at $3.75 per share, raising net proceeds of $104.8 million with Jefferies as the lead bookrunner (Jefferies would subsequently initiate coverage of Opko with a Buy rating in November 2011).34 In August 2011, Opko invested in a company called Neovasc (TSXV: NVC) to develop “unique” devices to treat cardiovascular disease. So far in 2013, Neovasc has generated operating losses of C$4.8 million and has a book value of just C$7.4 million.35 In October 2011, Opko acquired Claros Diagnostics, a company working on a small blood analyzer. This has become one of Opko’s main assets and is discussed further below. In December 2011, Opko acquired FineTech, an Israeli manufacturer of active pharmaceutical ingredients that are then sold to other drug companies. This business had book value of $10.9 million and was generating around $8 million in annual revenues at the time of acquisition.36

31 See Opko 9/30/13 10-Q (page 20)
32 See Opko 2011 10-K (page 6)
33 See Opko 2011 10-K (page 46)
34 See Opko 2011 10-K (page 46)
35 See Neovasc financial statements dated 9/30/13 (pages 2 and 4)
36 As of 9/30/11, per 8-K/A filed 1/25/12
In **January 2012**, Opko acquired a license (for no upfront payment) from a group out of Finland called Arctic Partners for an exploratory prostate cancer screening test. This has also become one of Opko’s main assets and will be discussed further below. Also in **January 2012**, Opko acquired a second Chilean pharmaceutical distribution business for $4 million. In **February 2012**, Opko invested in a small cap stock called ChromaDex (CDXC) and acquired a license for the distribution of its products in Latin America. Also in **February 2012**, Opko invested in a small cap stock called BioZone Pharmaceuticals (BZNE). Since that time, BioZone’s stock has fallen by more than 80%. In **March 2012**, Opko and the Scripps Institute announced a license agreement for a “novel” compound that blocks brain cell destruction in Parkinson’s Disease that at this point does not seem to be making much progress. In **June 2012**, Opko acquired a stake in a private Israeli company producing a hepatitis B vaccine. In **July 2012**, Opko entered into a license agreement with a Mexican professor of ophthalmology to treat macular edema, an opportunity that was never again mentioned by Opko. In **August 2012**, Opko acquired a Spanish company called Farmadiet Group for a total of $16 million. In **October 2012**, Opko acquired Prost-Data for $40 million, a CLIA lab to support the launch of the test acquired from Arctic Partners. In **December 2012**, Opko acquired a Brazilian pharmaceutical company, which the Company believed would help facilitate “the near-term commercialization in the Brazilian market of our 4Kscore™ [test].” One year has passed and the “near-term” Brazilian launch of the 4Kscore™ test has yet to happen.

**2013**

In **January 2013**, Opko acquired Cytochroma whose lead drug, Rayaldy, is seeking to treat secondary hyperparathyroidism in patients with chronic kidney disease. This has become one of Opko’s main assets and is discussed further below. In March 2013, Opko invested in a microcap public company called RXi (RXII) that is working on RNAi-targeted technologies and also sold certain assets to RXi. Since the transaction was announced, RXi’s share price has fallen almost 30% and the company’s market cap is below $40 million. In April 2013, Opko acquired a stake in OAO Pharmasynthez (MICEX: LIFE), a small Russian life science company. In **April 2013**, Opko announced the acquisition of Prolor Biotech, a Frost-backed public company working on a Phase 3 long-acting human growth hormone. This also is considered one of Opko’s main assets today and will be discussed further below. Most recently, in **October 2013**, Opko made an investment in a private company called Zebra Biologics, where Dr. Richard Lerner (an Opko board member) is also a director and founder of the company.

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37 Based on 12/6/13 closing price of $0.64, stock has fallen 83% since its closing price of $3.69 (on 2/27/12)
38 See Opko 3/31/13 10-Q (page 17)
39 See Opko 9/30/12 10-Q (page 27)
40 Based on 12/6/13 closing price of $2.99, stock has fallen 31% since its closing price of $4.35 (on 3/6/13)
C.) Poor Financial Results… Yet A Soaring Market Capitalization

Opko has lost money every year since it was formed, with losses increasing to $44 million in the first nine months of 2013.

**OPERATING LOSSES**

![Bar chart showing operating losses from 2007 to 9 mos '13](chart.png)

Other than the cash raised from investors, Opko has no net tangible assets. Tangible book value, excluding cash, amounted to negative $0.41 per share as of September 30, 2013:

<table>
<thead>
<tr>
<th>9/30/13 Shareholders’ Equity</th>
<th>$871 million</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less: Goodwill</td>
<td>- $222 million</td>
</tr>
<tr>
<td>Less: Other Intangibles</td>
<td>- $871 million</td>
</tr>
<tr>
<td>Plus: Carrying Value of Convertible Notes</td>
<td>+ $209 million</td>
</tr>
<tr>
<td>Less: Cash Raised from Investors</td>
<td>- $181 million</td>
</tr>
<tr>
<td>Tangible Book Value Excluding Cash Raised</td>
<td>- $194 million</td>
</tr>
<tr>
<td>Divided by: Fully-Diluted Shares Outstanding</td>
<td>/ 470 million</td>
</tr>
<tr>
<td><strong>Tangible Book Value Per Share, Excluding Cash</strong></td>
<td>- $0.41 per share</td>
</tr>
</tbody>
</table>
But the market has been forgiving to Opko, allowing it to continually increase its share count from 201 million fully-diluted shares at formation to nearly 470 million shares today:

9/30/13 Common Shares Outstanding 408.9 million
Plus: Shares to be Issued for Convertible Note 22.4 million
Plus: Opko Options Outstanding (via Treasury Method) 10.5 million
Plus: Opko Warrants Outstanding (via Treasury Method) 22.3 million
Plus: Prolor Options Outstanding (via Treasury Method) 5.8 million
F"ully-Diluted Shares Outstanding 469.9 million

FULLY-DILUTED SHARES OUTSTANDING

<table>
<thead>
<tr>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>Current</th>
</tr>
</thead>
<tbody>
<tr>
<td>($0.03)</td>
<td>($0.06)</td>
<td>$0.06</td>
<td>($0.01)</td>
<td>($0.01)</td>
<td>($0.00)</td>
<td>($0.41)</td>
</tr>
</tbody>
</table>

(in millions)
As a result of the significant increase in shares outstanding and the sharp recent rise in Opko’s shares, the Company’s fully-diluted market capitalization has increased from under $1 billion just two years ago to a current level of $5 billion (470 million shares x $11.10 per share price).

FULLY-DILUTED MARKET CAPITALIZATION

D.) Latin American Drug Distribution: The Majority Of Revenues… But No Profit And No Real Value

In 2009 and 2010, Opko acquired two Latin American generic drug distribution companies for $20 million ($0.04 per Opko share), forming the basis for this business. The base Opko business saw organic revenue growth of less than 1% in 2012, with gross profit dollars declining over 3%. Although this business has historically accounted for the majority of Opko’s revenues, it is tiny and appears to be challenged, with an annualized gross profit of only around $10 million. After a reasonable allocation of SG&A, it is unlikely this business even makes a profit.

No matter how one views Opko’s distribution business, it does not have any material value to Opko’s shareholders in the context of 470 million fully-diluted shares outstanding and a $5 billion fully-diluted market capitalization.

41 Mexico operations acquired in February 2010 for $3.5mm ($1.5mm cash and $2mm stock); Chile operations acquired in October 2009 for $16mm cash (see page 60-61 of 2010 10-K)
42 Calculated as 2012 revenues of $47.0mm less $6.1mm from Farmadiet acquisition less $7.1mm for FineTech acquisition less $5.0mm from ALS acquisition and $0.6mm from SciGen acquisition (June 2012) for 2012 “organic” revenues of $28.2mm vs 2011 reported revenues of $28mm (see 2012 10-K, page 56)
43 Calculated as 2012 gross profit of $19.2mm less $3.4mm from Farmadiet acquisition less $5.4mm from FineTech acquisition for “organic” gross profit of $10.4mm vs 2011 reported gross profit of $10.7mm (2012 10-K, page 56)
44 Estimated 2012 gross profit for “core” business of $10.4mm based on total Opko 2012 gross profit of $19.2mm less $3.4mm contribution from Farmadiet acquisition less $5.4mm contribution from FineTech acquisition (see pages 56 and 68 of 2012 10-K)
E.) Exploratory Alzheimer’s Diagnostic Test: The Mostly Highly Touted Opko Asset Just One Year Ago!

The Alzheimer’s Test essentially was the source of all investor interest in Opko in 2012 with the analyst at Ladenburg Thalmann predicting that the market could “approach $3 billion annually.”\(^{45}\) This test was acquired for what appears to have been essentially no upfront consideration in a license agreement with the University of Texas-Southwestern in 2009. The basic idea was a blood test that could diagnose Alzheimer’s (currently the only definitive diagnosis is autopsy). Dr. Thomas Kodadek, originally at the University of Texas-Southwestern, but now at the Scripps Institute (where he devotes 20% of his time to Opko as a consultant), developed the idea from a study he conducted of six patients with advanced Alzheimer’s and six healthy patients. He found specific antibodies that were prevalent in the Alzheimer’s group only, which would conceivably allow for the diagnosis of Alzheimer’s.

We have always doubted that the Alzheimer’s test would ever have significant commercial value. The study done by Dr. Kodadek was very preliminary and importantly, did not measure Alzheimer’s patients without clinical symptoms. It is very unclear whether the antibodies discovered even exist during earlier stages of the disease (if not, the test would be rendered fairly useless). Further, intellectual property remains uncertain, with a similar study conducted by a doctor at the University of Medicine and Dentistry of New Jersey. Even if the test were successful, there are likely other antibodies associated with Alzheimer’s that could be used as the basis of competing tests. As stated by a spokesman for the Alzheimer’s Association in August 2011, “Many labs are looking at this. They are all in the very preliminary, very early stages.” Also, the test’s value would likely be limited in the absence of an effective treatment for Alzheimer’s disease. By Dr. Kodadek’s own admission in a January 2011 interview, “it’s unclear whether people would want to know a couple of years ahead of time they are going to get Alzheimer’s if they can’t do anything about it.”

As recently as the 2011 10-K, the Company called the Alzheimer’s test its “lead program” and stated the following regarding commercialization: “We are currently conducting a broader validation study that we expect to be completed by mid-2012 and we expect to begin marketing our test for Alzheimer’s disease in 2013.”\(^ {46,47}\) As it turns out, the Alzheimer’s test has not proven to be as good as the initial study (which, as mentioned, was based on just six Alzheimer’s patients). The Company continued touting the test and in a September 2012 article, Frost argued they are still working to improve the sensitivity “in various ways” and think they will have a “valuable test.” Today, the Company appears to have moved on, downplaying the test’s significance. Again, this was basically the whole company one year ago.

\(^{45}\) See Ladenburg Thalmann initiation report dated July 14, 2011 (page 2)
\(^{46}\) See Opko 2011 10-K (page 6)
\(^{47}\) See Opko 2011 10-K (page 6)
The Jefferies analyst recently noted the Company “maintains its work on Alzheimer’s disease and cancer … however, there does not appear to be significant progress for potential launches of the Dx as previously expected.”\(^{48}\) Previously, the Jefferies analyst assigned $3 per share ($1 billion at the time) to this business.\(^{49}\) Today, it has been removed from her net asset value calculation given the test’s apparent failure (and the value has been made up by increasing the value of the other businesses).\(^{50}\)

**F.) Claros Diagnostics: Coming To A Doctor’s Office Near You In 2012… No, 2013… Make That 2014… Just Wait Until Q3 2015**

Opko acquired [Claros Diagnostics](#) in October 2011 in an auction process for $30 million ($10 million in cash, $20 million in stock and up to an additional $19 million in stock subject to achievement of certain milestones).\(^{51}\) Per its financial statements as of December 31, 2010, Claros had total assets of just $557,151 and had spent a cumulative $4.9 million on R&D since inception.

The basic concept was to have a small blood test system that can be used to run tests in-house during a visit to the doctor without having to wait for results from a lab. There are considerable challenges to broad adoption for this system. Our research has indicated that a lot of doctors do not want to deal with the paperwork associated with in-house lab testing. Also, as one doctor told us, “the reimbursement needs to be more lucrative to spend 10 minutes on lab work vs. 10 minutes with another patient.”\(^{52}\) Another problem is having a large enough test offering in order to incentivize people to invest in your platform. According to a different doctor we spoke with, you “absolutely need to get a lot of tests on these things before people will adopt. They could launch with just the PSA [prostate specific antigen] but won’t get a lot of uptake.”\(^{53}\)

Two full years since it was acquired, the product seems to be going nowhere. In June 2010 (even before the acquisition by Opko), Claros was “preparing for the European launch” of its point-of-care prostate test but it has generated no sales at this point. In December 2011, Opko put out a press release stating that they were commencing a multi-center clinical study of point-of-care test for PSA. They also stated “Opko intends to submit its application to the U.S. Food and Drug Administration for approval of the assay in 2012.” At a Lazard conference in November 2011, former Claros CEO Mike Magliochetti (who has since left Opko), stated that they would launch the product in Q1 2012 in Europe and hopefully by end of year 2012 in the U.S.\(^{54}\)

\(^{48}\) See Jefferies note dated October 29, 2012 (page 1)  
\(^{49}\) See Jefferies report dated August 10, 2012 (page 1)  
\(^{50}\) Jefferies report dated August 10, 2012 assigned “~$3/sh for AD/cancers Dx” but next report on October 29, 2012 assigned no value for Alzheimer’s test  
\(^{51}\) See [Opko 9/30/11 10-Q](#) (page 26)  
\(^{52}\) Based on discussions with a neurologist on November 15, 2011  
\(^{53}\) Based on discussions on November 7, 2013  
\(^{54}\) Per discussions with company at Lazard conference (November 15, 2011)
As soon as the 2011 10-K was released, the timing began to slip:

“As soon as the 2011 10-K was released, the timing began to slip:

“...we intend to launch the PSA test in Europe in the second half of 2012... We intend to submit our application to the Food and Drug Administration (the “FDA”) for clearance of the PSA test in 2012 and expect to begin marketing the test in the U.S. in 2013.”

And then one year later, things slipped again… in the 2012 10-K, Opko includes a complete cut and paste of the prior year’s language but with all of the dates pushed back exactly one year:

“...we intend to launch the PSA test in Europe in the second half of 2013. We intend to submit our application to the Food and Drug Administration (the “FDA”) for clearance of the PSA test and expect to begin marketing the test in the U.S. in 2014.”

At an appearance on CNBC’s Mad Money on January 28, 2013, Jim Cramer asked Dr. Frost about the Claros PSA test, to which he responded, “We’re further along but we want to get it perfect because it’s so big so we’re going to do another trial and I would predict, trying to be a little more conservative, that it will come to market at the end of the year.” It is now the end of the year and there is no test on the market so this proved to not be “conservative” enough.

The Company’s September 2013 presentation discussed initial Claros product offerings and said that for the PSA test that “U.S. FDA expected 2014,” which would seem to imply a 2015 U.S. launch:

A later slide in the presentation seemed to show the PSA launch in the U.S. ranging anywhere from Q4 2014 to Q3 2015:

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55 See Opko 2011 10-K (page 7)
56 Per Opko 2012 10-K (page 7)
57 Comments start at about 4 minutes, 50 seconds into the interview with Jim Cramer
And these September slides seemed to be later than what was indicated in the June slides presented at the Jefferies conference, which would indicate a Q2 2014 PSA test launch for Claros:

So what has happened that has led to these problems? According to our discussions with the Company and a physician closely tracking the progress of Claros, the product isn’t working as it has a high failure rate.\(^{58,59}\) This doesn’t mean that it is getting false positives – in too many

\(^{58}\) Per discussions with company at Jeffries conference (June 4, 2013)

\(^{59}\) Based on discussions on November 7, 2013
cases, you simply get an “error” reading with no result at all. Even the Company admitted that they stopped the PSA trial on the Claros due to error messages and stated that they “need more robust manufacturing.” In June 2013, they said they would start a new, six-month trial in the “next few months.”

Even assuming they can fix the problems with the Claros machine, one physician close to Claros did not see a huge market opportunity. He believed the probability Claros ultimately gets to $20 million in sales is around 50% and that there is “maybe a 5% chance they could get to $100 million in sales.” He also thought that if it were “a big market opportunity, people would have jumped on this a long time ago.”

It is now rather clear to us how Opko acquired this technology for just $30 million in a competitive auction. Even if they managed to one day get the machine working, it is hard to see how it would have material value in the context of a $5 billion market capitalization company.

G.) 4KscoreTM Exploratory Prostate Cancer Screening Test: “…24% Of All Cancers And 14% Of High-Grade Cancers Would Be Missed”

In January 2012, Opko put out a press release announcing the “acquisition of an exclusive license from a small group called Arctic Partners Ab Oy (Turku, Finland) for two biomarkers in the kallikrein family which, used together with prostate specific antigen (PSA), can reduce the need for prostate biopsies by over 50%.” Then in March 2012, there was another press release where the Company announced the exercise of a right of first refusal “to secure additional proprietary information, patents, know-how, property and technology associated with time-resolved fluorescence detection technology, which is directly applicable to the novel prostate cancer biomarkers.”

Opko appears to have paid nothing upfront for this license. As background on the technology, individuals associated with Arctic Partners presented data in May of 2010 (roughly two years before it was acquired by Opko) showing the so-called Four-Kallikrein panel’s (hence 4K) ability to reduce unnecessary biopsies. However, an accompanying editorial in the same issue raised serious questions around the value of such a test. Key arguments of the editorial include:

- “while use of the kallikrein panel advocated in the study may reduce the number of biopsies performed, it also seems to reduce overall cancer detection”;
- “…24% of all cancers and 14% of high-grade cancers would be missed”;
- “…high-grade cancers might actually be missed with more frequency than the authors estimate”; and
- “…it seems unlikely that a strategy which misses some high-grade and potentially aggressive tumors would actually optimize screening.”

60 Per discussions with the Company at Jefferies conference (June 4, 2013)
61 Per discussions on November 7, 2013
From a more common sense standpoint, one may want to ask: if this test is such an incredible breakthrough, then why did no one attempt to commercialize it for two years after the study was published? And, why was Opko able to sign a licensing deal for seemingly no consideration?

In May 2012, Opko signed an agreement with International Health Technology (IHT) to offer the 4Kscore™ test in the UK, Ireland, Sweden and Denmark. In October 2012, Opko issued a press release announcing that IHT had “launched the Opko 4Kscore™ in Europe as part of IHT’s ProstateCheck™ program.” While technically correct, Opko appears to be overstating the true market coverage. Opko’s 2012 10-K indicates that the test was only launched in the UK (not all of Europe): “In October 2012, our strategic partner, International Health Technology, Ltd. (“IHT”), launched sales of lab services using this novel panel of biomarkers in the United Kingdom as part of IHT’s ProstateCheck™ program.”

The test has now been on the market for one full year and there has been no disclosure in Opko’s 10-K or subsequent 10-Q’s regarding initial sales in the UK. Given that Opko specifically breaks out revenue contributions from several recent acquisitions, including one that contributed as little as $600,000 in revenues during 2012, we think this highlights a fairly limited interest in this test. In fact, our discussions with physicians in the UK confirmed a low level of interest and we only heard mention of some use in a few London private practices.

Also in October 2012, Opko announced that it was acquiring Prost-Data (OURLab) a CLIA lab. At the time, Dr. Frost stated, "The addition of OURLab to the Opko family will support the early launch of the important 4Kscore™ prostate test as a laboratory-developed test in the U.S. and complements the Company's recent European commercial launch of the 4Kscore™ through its UK-based partner, International Health Technology, as part of its ProstateCheck™ early prostate cancer detection service." A year since talk of this “early launch,” we have seen no sales out of the U.S. and apparently no material sales in Europe. Prost-Data’s sole shareholder was Dr. Jonathan Oppenheimer (OURLab stands for Oppenheimer Urologic Reference Laboratory), who according to the Opko press release, was to become CEO of Opko’s diagnostics division. We have some concerns related to Dr. Oppenheimer’s past. In late 2000, he lost a lawsuit in what the New York Times reported “…may well represent the first time in the United States that a jury imposed a substantial libel award against a defendant who published an anonymous Internet message.” The jury’s verdict awarded Dr. Sam Graham $675,000 in compensatory and punitive damages after Dr. Oppenheimer posted a message on a Yahoo! Message Board under the name “fbiinformer” accusing Dr. Graham of taking a kickback from Urocor, a company that provides pathology services to hospitals (Dr. Oppenheimer used to work at Urocor). According to a Forbes article published at the time, “It wasn’t true, and Oppenheimer had never even met Graham. Nor did he have anything against Graham. But Oppenheimer was trying to get business for his own laboratory and spreading the rumor about Graham was his way of

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62 See Opko 2012 10-K (page 7)
63 Opko disclosed that SciGen contributed “$0.6 million of revenue” in its 2012 10-K (page 56)
disparaging Urocor, a competitor. Graham, who has since moved on to a private practice in Virginia, simply got in the way, according to Alan Rudlin, Graham’s lawyer.” And according to an ABC news article from the time, the judge in the case “called the anonymous attack ‘about as despicable as any course of conduct that one could engage in.’”

On November 7, 2012, Dr. Frost appeared on Mad Money to discuss the 4Kscore™ test. Even host Jim Cramer acknowledged that “Opko is only for speculation. It's very risky.” During the interview, Dr. Frost claimed that “we can be on the market within months.” At that point Cramer asked, “this is a 2013 product, right Dr. Frost,” to which he responded, “It could be very early 2013, yes.” Dr. Frost then stated, “by the way, it’s already on the market in the UK. We just introduced it a month ago or so and now we’re going to have all of our subsidiaries in Spain and Latin America start to market in those locations so this is a major effort on our behalf now.”

We have heard nothing since then on the launches in Spain and Latin America. It’s been a year and they appear to be nowhere on any of the claims from that interview.

In December 2012, Opko acquired a Brazilian pharmaceutical company that, according to Dr. Frost, “…facilitates the near-term commercialization in the Brazilian market of our 4Kscore™, a novel panel of biomarkers and associated algorithm to more accurately detect and grade possible prostate cancers.” One year later, we have heard nothing about any Brazilian 4Kscore™ revenues.

Also, on January 28, 2013, Dr. Frost again appeared on CNBC’s Mad Money and stated, “we’re going to be marketing [the 4Kscore™ test] within the next two to three months in the United States.” It has now been ten months and there is no test being marketed in the U.S.

In May 2013, Opko announced its Q1 operating and financial highlights. In the press release, Opko claimed to be “Preparing for 4Kscore™ Commercial Launch” and stated that “development work toward the U.S. commercial launch of the Opko 4Kscore™ prostate cancer test as a laboratory developed test through our CLIA-certified laboratory based in Nashville, TN, remains on track for a 2013 launch.” However, just three months later, in August 2013, the Opko Q2 operating and financial highlights section stated: “the U.S. commercial launch of the Opko 4Kscore™ prostate cancer test as a laboratory developed test will be through our CLIA-certified laboratory based in Nashville, TN.” Note that the language is almost identical except for the removal of the “remains on track for a 2013 launch” language.

We believe reimbursement will also be a large problem with Opko’s strategy as they are trying to launch the test initially as a laboratory developed test (LDT). Laboratory developed tests are regulated under federal laws known as the Clinical Laboratory Improvement Amendments (CLIA). They are overseen not by the FDA, but by the Centers for Medicare and Medicaid Services (CMS). Therefore, these tests are not FDA approved and federal law doesn’t even

64 Comments start about 5 minutes, 5 seconds into the interview with Jim Cramer
65 Comments start about 5 minutes into the interview with Jim Cramer
require that labs provide validation studies for laboratory developed tests to CMS, allowing these tests to get to market with a much less rigorous process.

The government is considering stronger oversight of these tests given examples of problematic LDTs. Laboratory developed tests are typically brought to market to satisfy a testing niche that is not served by a commercially available test. There are currently two ways to bring an LDT to market:

- The manufacturer sets up its own CLIA-certified lab. The company then develops its test kits and performs all testing within that lab; or

- The manufacturer pursues premarket approval or 510(k) notification in order to offer the LDT kits for sale outside of the lab in which they were developed. Once the FDA has approved an LDT via this process, that test can then be assigned a CLIA classification, assembled into a kit and sold to labs with matching CLIA accreditation.

So, the near-term hope for the 4Kscore™ test is that Opko will design the test out of its recently acquired CLIA lab in Nashville. They will then have the small sales force that is employed by the lab go out and try to get urologists to use the 4Kscore™ test which will be processed at the Opko lab. Developing an LDT with no real clinical data will make it very difficult to get insurance coverage. They will be limited to people who will pay out of pocket which severely reduces the market opportunity (and likely the price that can be charged for the test).

Here is a June 2013 investor presentation (Jefferies conference) that highlights “U.S. LDT in 2013” for the 4Kscore™ test:

**OPKO Diagnostics — Initial Applications**

- **Total-PSA, Testosterone Point-of-Care tests**
- **Next Generation Prostate Cancer Markers (4KScore™):**
  - Combines PSA, free PSA, intact PSA and human kallikrein 2 markers as a Laboratory Developed Test (LDT) with the goal of significantly greater accuracy
  - Markers tested in over 10,000 patients to predict the probability of cancer-positive biopsy and reduce unnecessary biopsies

<table>
<thead>
<tr>
<th>Market Opportunity</th>
<th>Projected Launch</th>
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<tbody>
<tr>
<td>WW: 70 million PSA tests annually</td>
<td>Currently marketed in UK</td>
</tr>
<tr>
<td>&gt;1 million prostate biopsies per year in U.S., &gt;750,000 are unnecessary</td>
<td>U.S. LDT in 2013</td>
</tr>
<tr>
<td>Costs in excess of $2.5 billion</td>
<td>POC platform by 2014/15</td>
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- **Vitamin D Point-of-Care Test**

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<thead>
<tr>
<th>Market Opportunity</th>
<th>Projected Launch</th>
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</thead>
<tbody>
<tr>
<td>WW market: 100 million tests annually (70 million U.S.)</td>
<td>POC platform</td>
</tr>
<tr>
<td>WW market size: about $8 billion</td>
<td>• EU by Q1 2014</td>
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<td></td>
<td>• U.S. by Q4 2014</td>
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Here is a September 2013 investor presentation that claims a Q4 2013 launch as LDT (though the 2013 language had already been removed from August 2013 press release as noted above) and point-of-care test “4-5 years” later:

**Next Generation Prostate Cancer Testing – 4KScore™**

The 4KScore™ address a critical unmet need in Prostate Cancer care:

- Current screening (based on PSA) leads to over-biopsy and over-treatment
  - PSA lacks predictive accuracy in the “grey zone” (3-10ng/mL) due to false positives (up to 75%)\(^{(1)}\)
  - >1 million annual biopsies in the US, 750,000 are negative\(^{(2)}\)
  - 4.2% of biopsies result in a complication that require an inpatient admission\(^{(3)}\)
- 4Kscore™ provides prostate cancer risk assessment based four blood based biomarkers:
  - Total PSA (tPSA)
  - Free PSA (fPSA)
  - Intact PSA (iPSA) – the subset of free PSA with a preserved bond at Lys145-Lys146
  - Human kallikrein 2 (hK2) – also known as kallikrein-related peptidase 2
- Validated across multiple patient cohorts predict cancer before biopsy
  - Retrospective tests in over 10,000 patients
  - Shows >80% accuracy in predicting prostate cancer
  - Can eliminate 50% of prostate biopsies

**OPKO 4KScore™ strategy**

- Laboratory Developed Test in the US with a planned Q4 2013 introduction
  - $300 million market size as a new lab test before the first biopsy
- FDA-cleared point-of-care test on the Clarus-1 System in 4-5 years
  - Will compete as an alternative to total PSA alone in the US $1B PSA market

In summary, the 4Kscore™ test:

- was acquired from a small, obscure group out of Finland for no upfront payment;
- has gone over three years without anyone commercializing it;
- has been significantly delayed;
- has been launched in the UK but is apparently not really seeing any traction;
- is based on questionable science (see editorial);
- is supposed to be launched out of a small lab in the U.S. with a tiny sales force that will likely have a hard time canvassing a large population of urologists; and
- patients will most likely need to pay out of pocket for the test.

**H. Rayaldy:** “I have probably 500 [CKD] patients in my clinic… maybe 4 or 5 of them could benefit from switching to CTAP101”

In January 2013, Opko announced the acquisition of a company called Cytochroma for $100 million in stock and certain milestone payments. Cytochroma has two main products in development:
• CTAP101 (renamed Rayaldy): a vitamin D prohormone to treat secondary hyperparathyroidism in patients with Stage 3 or 4 chronic kidney disease and vitamin D insufficiency (Phase 3 results are expected in the first half of 2014)${}^{66}$

• Alpharen (Fermagate Tablets): a non-absorbed phosphate binder to treat hyperphosphatemia in dialysis patients (Phase 3 results in the first half of 2017)${}^{67}$

The most important drug and main focus of Opko at this point is Rayaldy. According to Cytochroma’s presentation at the time of the Opko acquisition, they believed the drug could enter the market in 2016. Rayaldy is targeting patients with secondary hyperparathyroidism (SHPT) in Stages 3 and 4 of chronic kidney disease (CKD). In the U.S., there are an estimated 7.6 million people with Stage 3 (moderate) chronic kidney disease (of which roughly 34% are believed to have SHPT). Many patients are not even aware that they have CKD and symptoms are normally subtle until later in the course of the disease. There are also roughly 400,000 Stage 4 CKD patients (severe) and about 300,000 stage 5 patients (kidney failure).

Many CKD patients develop secondary hyperparathyroidism (SHPT), which results from the increased production of parathyroid hormone (PTH) and develops primarily during Stages 3 through 5. SHPT develops in these patients when declining kidney function lowers phosphorous excretion, causing phosphorous levels to increase while calcium and vitamin D levels decline. As the kidneys are not converting sufficient amounts of vitamin D to its active form and are not adequately excreting phosphate, this leads to hypocalcemia and increases in PTH secretion (in an attempt to increase calcium levels). This process both weakens the bones and puts extra pressure on the blood vessels, with the potential for bone disease and cardiovascular problems in the patients.

To treat these patients, physicians generally start with dietary changes. After that, they will primarily use nutritional vitamin D and phosphorous binders. Vitamin D helps bring down the parathyroid hormone (PTH), with inexpensive over-the-counter and generic prescription products (such as ergocalciferol or calcitriol) both widely used. The side effect of vitamin D is that it can raise calcium and phosphorous too much, which can become a problem in later stages of CKD (when the kidneys are really struggling). So in more advanced stages of treatment, physicians switch patients to other vitamin D analogs such as Zemplar and Hectorol. These treatments have the beneficial effect of bringing down PTH without bringing up calcium levels.

The following are the existing treatments on the market for treating SHPT:

• Over-the-counter vitamin D for early treatment in Stages 3 and 4 CKD

• Hectorol (Genzyme/Sanofi), which comes off patent in 2014${}^{68}$

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66 See Opko September 2013 investor presentation (page 7)
67 See Opko September 2013 investor presentation (page 7)
• Zemplar (Abbott), which also comes off patent in 2014 (Teva has already launched a generic zemplar capsule)

• Calcitriol (a generic product) and off-label usage of another generic product called Drisdol (generic is ergocalciferol)

Even if Rayaldy is approved and commercially launched in 2016, we believe there is limited need for new SHPT treatments. Rayaldy will need to compete with both OTC vitamin D and generic vitamin D analogs when Hectorol and Zemplar come off patent next year (before Opko even hopes to complete its studies).

We have spoken with numerous nephrologists who treat patients with SHPT and the tone was skeptical. For example, Dr. Jeffrey Giullian, a veteran nephrologist who has about 500 CKD patients in his clinic, had the following to say when we discussed Rayaldy/CTAP101 and its market potential with him:69

“In Stage 3 and 4 chronic kidney disease, you don’t really see the side effects of giving OTC vitamin D ... there’s the rub ... you can give OTC or calciferol without the side effects. It’s later when the kidney is struggling that the nutritional vitamin D causes the side effects, but at that point we’re switching over to the analogs [such as Zemplar or Hectorol]. So it’s hard for me to see a niche for CTAP101 ... in early stages of treatment you can use nutritional vitamin D and in later stages you want to use Zemplar or Hectorol.

I would think they [Cytochroma] are overstating the market opportunity... I probably have 500 [CKD] patients in my clinic ... maybe 4 or 5 of them could benefit from switching to CTAP101.

The issue is this is a new drug that is just barely better than existing treatments that are over-the-counter and cheap. So would it justify a huge difference in cost, probably not.”

When asked about the likelihood of getting nephrologists to switch patients to Rayaldy/CTAP101:

“A non-inferiority trial isn’t going to get CTAP101 any traction ... why would I want something 10x more expensive that simply isn’t inferior? Would need to demonstrate superiority vs. an active control.”

And when asked whether his peers are excited about Rayaldy/CTAP101, “No, they’re not really talking about it.”

68 See Genzyme 2010 10-K (page 15)
69 Per discussion on November 6, 2013
In total, we surveyed 51 nephrologists to gauge the market opportunity for Rayaldy. Based on the responses we received, the surveyed nephrologists would switch just 9% of their patients to a therapy like Rayaldy if it were approved. At an annual cost of $1,500 per year, we believe the true sales opportunity for Rayaldy is below $150 million per year (~1 million estimated SHPT patients that are treated x 9% switched to Rayaldy x $1,500 annually). After selling and marketing expenses, we would not expect Rayaldy to ever be a major profit contributor to Opko.

You don’t have to take our word for it as even the perpetually bullish Jefferies analyst has her doubts on the market potential for Rayaldy. In her March 19, 2013 research note, she noted:

“According to nephrologists that we talked to, it appears that there is not significant unmet need in treating SHPT patients currently...

Cytochroma estimates ~$295M annual sales for oral Hectorol and Zemplar in predialysis settings. With Hectorol and Zemplar going generic in 2014, any new vitamin D analog with premium pricing would need to be far superior to capture significant market share, in our view...

Our nephrologists discussions indicate a majority of patients only with vitamin D insufficiency would be adequately treated with OTC vitamin D supplements...

Nephrologists note that for vitamin D insufficiency, patients with SHPT can easily take OTC vitamin D supplements, along with generic vitamin D analog, rather than paying a premium for new vitamin D analogs...

...given that both Hectorol and Zemplar are going generic in 2014, our estimates could be viewed as aggressive.”

The Jefferies analyst estimated peak sales potential for Rayaldy at ~$350 million, well short of the patently absurd $12 billion market size that Opko touted in a recent investor presentation. And we believe the $350 million estimate is based on very aggressive pricing assumptions of $3,500 per patient for Rayaldy, even though Hectorol and Zemplar currently cost around $3,000 to $3,300 per year and that price will likely fall dramatically next year (before Opko even hopes to have completed Rayaldy trials) when both drugs go generic (as shown in the excerpts above, she acknowledges her estimates could be “aggressive”). For comparison, generic treatments such as calcitriol and ergocalciferol generally cost a few hundred dollars per year. Additionally, if approved, Rayaldy would have to compete with OTC vitamin D that can be bought at your local drugstore for around $5 per bottle ($50 to $60 per year).

70 Proprietary survey of 51 nephrologists completed on November 14, 2013
71 Calculated based on 8mm stage 3 + 4 CKD patients, of which 36% are assumed to have SHPT (34% of stage 3 and 74% of stage 4, per zemplar website). Estimated 1mm diagnosed prevalence for SHPT per GlobalData report titled “Hyperparathyroidism – Analysis and Market Forecasts to 2019” which implies 34% of stage 3+4 patients with SHPT are treated.
At our estimate of peak sales of no more than $150 million per year, we believe Rayaldy is worth at most $500 million or just $1 per Opko share. Even at this aggressive valuation, it would still represent a value of five times what Opko paid to acquire Cytochroma just a few months ago.

I.) Prolor Biotech: Even Their Management And Financial Advisors Are Skeptical

In April 2013, Opko announced the acquisition of Prolor Biotech (“Prolor”) for $480 million in stock. Prolor was a Frost-backed publicly-traded company that went public via reverse merger in May 2007. The company was originally formed as LDG Inc. in August 2003 and, on May 9, 2007, LDG Inc entered into an agreement and plan of merger/reorganization with Modigene. Also in May 2007, the company completed a private placement of 8.7 million shares and warrants (concurrent with the closing of the merger). An additional 5.4 million shares plus warrants were sold to four strategic investors led by Dr. Frost for a total consideration of $2 million (Frost and Hsiao were then appointed to the board upon closing of the transactions). Then, on May 21, 2007, an additional 155,673 shares of stock were issued to the Frost-led investor group for no additional consideration.\(^72\) The company’s name was changed to Prolor Biotech in June 2009. Additional capital raises occurred in March 2010, with a $24.4 million private placement (10.4 million shares at 17% discount to average 30-day closing price) and in May 2012 with the issuance of 7.5 million shares at $5 per share, raising $35 million.

The core technology for Prolor is its “CTP technology” (carboxyl terminal peptide) that can be attached to an array of existing therapeutic proteins to allow for a long-acting formulation (and therefore, once per week injections instead of daily). Prolor has an exclusive license to the technology, which was developed at Washington University in St. Louis, in all but four endocrine proteins: FSH, LH, TSH and hCG (these are licensed to a company now owned by Merck). Merck markets a drug branded Elonva (follicle-stimulating hormone, FSH, used as a fertility treatment) based on the technology.\(^73\)

In a May 2012 investor presentation, Prolor claimed it was going to initiate a Phase 3 study for hGH-CTP by December 2012.\(^74\) However, by a December 2012 investor presentation, they indicated that they were on track for a Q1 2013 filing for adult Phase 3 trial program and that this was “only 3 months delay compared to original plan.”\(^75\) Per Opko’s Q2 2013 10-Q, “in June 2013, Prolor initiated a pivotal Phase III clinical trial for its long-acting version of human growth hormone, hGH-CTP, for treatment in adults with growth hormone deficiency (GHD).”\(^76\) So they finally got the trial launched, but seven months behind the mid-2012 expectations.

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\(^72\) Prolor history based on company history section of Prolor 2008 10-K (pages 1-2)
\(^73\) See Prolor 2012 10-K (page 2)
\(^74\) See May 2013 Prolor presentation (slide 16)
\(^75\) See December 2012 Prolor presentation (slide 7)
\(^76\) See Opko Q2 2013 10-Q (page 35)
The Phase 3 trial for adults consists of 189 patients in U.S., EU and Israel. Phase 3 results are expected in H2 2015 (per Opko’s September 2013 investor presentation).\(^77\) For pediatric use, a Phase 2 trial is ongoing with Phase 3 results expected in H1 2018.\(^78\)

Unfortunately for Opko, Prolor has been beaten to the punch by LG Life Sciences, who will likely have a nearly identical drug on the market next year, before Prolor will even complete its trials. LG Life Sciences has been producing growth hormone Declage since 2007. Per LG’s Q2 2013 investor presentation, you can see that they have completed Phase 3 trials in their SR-hGH (slow-release human growth hormone) and have filed an NDA:

Additionally, LG and partner BioPartners received EU approval for the drug in August 2013 and announced they were “…the first company to receive a marketing authorisation in the EU, Norway and Iceland for a prolonged-release formulation of recombinant human growth hormone (rhGH) which will cut the number of self-administered injections from once-a-day to once-a-week - a major breakthrough in rhGH treatment.”

While further behind, even Teva Pharmaceuticals appears to be focused on the long-acting market, having moved into Phase 2 for a long-acting human growth hormone (Teva also produces Tev-Tropin, a short-acting HGH drug currently on the market).\(^79\)

\(^{77}\) See September 2013 presentation (slide 7)

\(^{78}\) See September 2013 presentation (slide 7)

\(^{79}\) See Teva Q2 2013 earnings call transcript from August 1, 2013
A read of the Prolor/Opko merger proxy reveals how little interest the Prolor assets seemed to generate in the marketplace. In the “Background of the Merger” section, Prolor disclosed that it was “engaged in extensive discussions and negotiations with a pharmaceutical company, which we refer to as ‘Bidder A,’ regarding a potential acquisition of Prolor by Bidder A.” Dr. Frost is a director of and deemed an affiliate of Bidder A. These discussions took place between October and December 2012 and given that they disclosed Frost was a board member of “Bidder A,” it is almost assuredly Teva.

According to the proxy, Teva appears to have walked away after diligence:

“Following extensive due diligence by Bidder A, including site visits at the facilities of Prolor and its suppliers, Bidder A determined not to proceed with an acquisition of Prolor and suggested to Prolor that the parties focus their future discussions on the licensing by Prolor to Bidder A of specific applications of Prolor’s technology. Over the following months, Bidder A’s and Prolor’s respective management teams engaged in continued discussions regarding potential licensing arrangements; however, Prolor and Bidder A did not reach a definitive agreement regarding any such arrangement.”

So at that point, it appears the focus turned to a merger of Opko and Prolor, with no other bidders expressing any serious interest in Prolor.

Also interesting is what the proxy says about management’s own views of its prospects and the sales of its hGH-CTP drug. Using Prolor management’s projections, Oppenheimer (the financial advisor to the special committee of Prolor’s board) performed a net present value analysis of Prolor’s various assets. Here are the results of their analysis (see pages 68-69 of the proxy):

<table>
<thead>
<tr>
<th>Source of Value</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>hGH-CTP</td>
<td>$130.5—$173.9</td>
</tr>
<tr>
<td>Factor VIIa</td>
<td>$18.6—$23.9</td>
</tr>
<tr>
<td>GLP 1/6030</td>
<td>$29.6—$41.0</td>
</tr>
<tr>
<td>Net Operating Loss Carry Forwards</td>
<td>$13.0—$15.0</td>
</tr>
<tr>
<td>Cash &amp; Equivalents</td>
<td>$29.9—$29.9</td>
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<tr>
<td>Total Debt</td>
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<tr>
<td>Equity Value</td>
<td>$221.6—$283.7</td>
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<tr>
<td>Fully Diluted Shares Outstanding</td>
<td>66.7—67.1</td>
</tr>
<tr>
<td><strong>Implied Equity Value per Share</strong></td>
<td><strong>$3.32—$4.23</strong></td>
</tr>
</tbody>
</table>

So, even the much touted Phase 3 opportunity is viewed by Prolor’s own management and its financial advisors as being worth only $131 million to $174 million, or just 2.6% to 3.4% of Opko’s current fully-diluted market capitalization.

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80 See proxy (page 48)
81 See proxy (page 49)
82 See proxy (page 49)
83 See proxy (page 69)
J.) A Web Of Stock Promotion That Should Concern Even The Most Brazen Investor

While Dr. Frost is a billionaire who has earned the admiration of the investment community after selling two companies (Key Pharmaceuticals and Ivax Corporation) for incredibly large gains, we also think there is another side of his career that should be of great concern to anyone investing in Opko. Dr. Frost has a disturbingly large number of connections to what we believe are two serial stock promoters that have each been the subject of multiple lawsuits, Barry Honig and Michael Brauser (who together run an entity called Marlin Capital).

We have counted 16 different penny stocks in which Frost, Honig and Brauser have all invested in recent years, including entities in which Opko is directly involved. In fact, the business address listed for Honig and Brauser, 4400 Biscayne Blvd., is owned by Dr. Frost and is also the offices of Opko Health, Ladenburg Thalmann (again, where Dr. Frost is Chairman) and numerous other companies in which Frost, Honig and/or Brauser are involved (including MusclePharm, BioZone, SafeStitch Medical, Non-Invasive Monitoring Systems and others). In fact, Barry Honig’s office is listed as being in the exact same suite (Suite 850) of 4400 Biscayne Blvd. as Dr. Frost’s Frost Gamma Investments Trust.84

We have found 38 different stocks connected to Barry Honig and 15 connected to Michael Brauser (there are likely many more, but this is what we could track down). Only three of these companies have a market capitalization above $150 million, only one of these companies generates a profit… (Pyramid Oil), which only makes around $1 million per year.85 Many of these companies have cost investors a significant amount of money and both individuals have been the subject of extensive litigation.

84 See Document Security Systems (DSS) filing (page 169)
85 Operating income of $975,064 in 2012 per 10-K (page 30)
## List of Opko, Frost, Honig and Brauser Holdings

<table>
<thead>
<tr>
<th>Ticker</th>
<th>Shares</th>
<th>Market Cap</th>
<th>Shares</th>
<th>% Out</th>
<th>Date</th>
<th>Shares</th>
<th>% Out</th>
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<th>% Out</th>
<th>Date</th>
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<td>10/1/13</td>
<td>5.5</td>
<td>7.5%</td>
<td>9/30/13</td>
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<tr>
<td>Chromedx (2)</td>
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<td>5.3</td>
<td>4.5%</td>
<td>12/31/13</td>
<td>7.5</td>
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<td>9/25/13</td>
<td>9.2</td>
<td>1.2%</td>
<td>11/15/13</td>
<td>4.2</td>
<td>1.2%</td>
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<td>Symmetry Therapeutics</td>
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<td>0.1%</td>
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<td>8/22/13</td>
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<td>5/31/13</td>
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<tr>
<td>Atro-Therapeutics</td>
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<tr>
<td>Iden</td>
<td>IEN</td>
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| Other Public Entities

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<tr>
<td>3/29/13</td>
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<td>5.4%</td>
</tr>
</tbody>
</table>

Note:
1. In August 2013, MSPL bought 32mm convertible plus warrants from BioZone; MSPL leases office space at 4400 Biscayne Blvd (Frost's building)
2. BioZone selling substantially all assets to MSPL and merging with Cricrysal Discovery
3. In December 2013, MSPL leased office space at 4400 Biscayne Blvd with Frost and Hsiao purchasing preferred stock in the deal
4. Frost, Honig and Brauser all own shares and Brauser's son is an executive
5. Frost/Honig/Brauser sued by BioZone original founder
6. MSLP leased office space at 4400 Biscayne Blvd (Frost's building)
7. EXCX becomes SAGE which becomes Pershing Gold (PGLC) - Honig on the board; was chairman of Sagebrush Gold
8. MusclePharm, Brauser, Honig and Frost Gamma were part of a $700,000 investment in November 2013 into Fuse Science
9. Frost/Honig/Brauser sued by BioZone original founder
10. Marlin Capital filed 13D on 10/5/11 owning 5.5% of the company (both Honig and Brauser signed filing)
11. Other Public Entities

Denotes companies in which Frost plus Honig and/or Brauser are involved

Source: Bloomberg, SEC filings
First, a company called Sunair Services Corporation (SNR) filed suit against Honig and Brauser (and others) in March 2009 for violations of federal securities laws. Here are some of the specifics from the lawsuit regarding Mr. Brauser’s background that Sunair believed should have been disclosed:

“…Specifically, Equifax alleged that Defendant Michael Brauser participated in the fraudulent creation of fictitious receivables and further participated in accounting overstatements that disguised Naviant’s true financial condition. 86

...Equifax alleges in the Federal Fraud Litigation that, in order to induce Equifax to enter into a merger with Naviant, Defendant Michael Brauser (a) hid low-priced “CPM” (Cost Per Thousand) e-mail transactions in order to inflate Naviant’s effective CPM rate, (b) maintained one set of books for Naviant that was more accurate and complete and another that omitted the low-priced e-mail transactions, which Naviant provided to Equifax and its accountants during merger negotiations, (c) misrepresented the volume and price of transactions that accounted for a large percentage of Naviant’s pre-acquisition revenue, and (d) engaged in fictitious transactions with other email marketing companies to inflate Naviant’s financial performance. 87

...Softbank Capital Partners (“Softbank”), a Naviant shareholder, sued Defendant Michael Brauser on March 24, 2008, in the Federal Fraud Litigation for breach of contract and indemnification for Defendant Michael Brauser’s failure to pay Softbank his share of the millions of dollars of attorney’s fees and costs incurred by Softbank in its capacity as the shareholders representative of Naviant. Softbank claims that “a substantial portion of Equifax’s claims were meritorious” and Defendant Michael Brauser had been “intimately involved in carrying out various frauds at Naviant and covering up their misdeeds through threats and intimidation.” Softbank also claims that Defendant Michael Brauser represented to Softbank that he was “judgment proof” as a result of transferring away all of his personal assets, with the exception of his Bentley automobile and personal computer... 88

... Defendant Michael Brauser also was sued on January 30, 2009, for fraud and breach of fiduciary duty in Kast v. The Tube Media Corp., 09-06285, in the Circuit Court for the 17th Judicial Circuit in and for Broward County, Florida (“State Fraud Litigation”), in connection with Defendant Michael Brauser’s role as a Director of The Tube Media Corp., a publicly traded company that ceased operation in October 2007. Specifically, Defendant Michael Brauser is accused of knowingly withholding payroll taxes from employees without remitting them to the government, filing materially false and misleading financial reports, and intentionally making misrepresentations of material facts. 89

86 Per Sunair SEC filing dated March 13, 2009 (page 6)
87 Per Sunair SEC filing dated March 13, 2009 (pages 6-7)
88 Per Sunair SEC filing dated March 13, 2009 (page 7)
89 Per Sunair SEC filing dated March 13, 2009 (pages 7-8)
Barry Honig was also sued in January 2011 in relation to Empire Sports & Entertainment (EXCX) by former two-time winning heavyweight champion Shannon Briggs. According to one article, “…Briggs filed a major lawsuit in New York State Supreme Court, alleging breach of fiduciary duty, conversion, unjust enrichment and breach of contract against Gregory D. Cohen, Shelly Finkel and Barry Honig, and their boxing and entertainment promotional company, Empire Sports & Entertainment.” Briggs claimed he was the “victim of a ‘ripoff’ on two fronts by his former promoters and business partners, part and parcel of which includes documents in which his signature was ‘forged.’” Financially, Briggs alleged that he had agreed to fight then world champion Vitali Klitschko for a purse of $750,000, “…but that he wound up with a mere $25,000, after he returned to the United States after the prolonged hospital stay in Hamburg. … ‘To add insult to injury,’ the lawsuit alleges, ‘the defendants deducted the cost of Briggs' hospitalization from the understated purse of the bout.’”

However, the story doesn’t end there. Empire Sports & Entertainment ultimately became Sagebrush Gold (SAGE) on June 1, 2011, with Barry Honig serving as Chairman. In October 2011, Honig announced to Sagebrush shareholders that “Legenday investor Dr. Phillip Frost (Chairman of Teva Pharmaceuticals, Inc., Ladenburg Thalmann & Co., Opko Health, Inc.) has invested $5 million in our subordinated debt and convertible preferred stock.” The company changed names once again and became Pershing Gold (PGLC) in March 2012. Today, Pershing Gold is 19.4% owned by Frost and 10.1% owned by Honig. Brauser had also previously been a shareholder but appears to have sold all of his shares in April 2013.90

If this isn’t enough, Adrian James (a well-known stock promoter involved in such companies as KWBT, SRGE, DHNA, POWN, PYTL, ZOWI and LYJN, to name a few) shows up as a shareholder of Pershing Gold and was hired by a company called Valor Gold (VGLD) in which Pershing Gold owned a stake. James’ involvement with Frost/Honig/Brauser entities appears to extend to Sagebrush Gold (before it became Pershing) and MusclePharm. As an interesting side note, Adrian James sued Jonathan Lebed, another well-known stock promoter associated with an entity he calls the National Inflation Association (NIA), for ripping off his “Stockumentary” and illegally using footage from his company’s stock promotion videos. In addition to being behind the spectacular rise and crash of Synacor (SYNC) in 2012, Lebed’s NIA had earlier heavily promoted a company called BroadVision (BVSN), an obscure company that briefly soared in early 2012 after the NIA began recommending the stock to its membership. Interestingly, in October 2011, before the NIA promotion began, Honig and Brauser’s Marlin Capital filed a 13D indicating a 5.5% ownership interest in the company. In its disclosure, the NIA stated that its co-founders “…have also been referred business in the past from somebody who has filed as a large BroadVision shareholder.”

Brauser and Honig were both involved in a company called SendTec (SNDN) which lasted traded for $0.0007 per share (that’s not a typo). Brauser resigned as Chairman in September

90 See prospectus dated 4/2/13 (page 3)
2006 and in November 2006, a class action suit was filed against the company and individuals including both Michael Brauser and Barry Honig.

Opko itself is involved with the penny stock trio through its ownership of 10.9% of BioZone Pharmaceuticals (BZNE). Currently, Frost owns 14.5% of the company, Honig owns 7.9% and Brauser owns 6.8%. Here are some facts about BioZone:

- The value of this investment to Opko is minimal, as BioZone’s total market cap is just $40 million and the company generated just $2 million of revenues last quarter (which was down 56% from the prior year);

- Since Opko announced its investment in BioZone in February 2012, the stock is down ~80%;91 and

- The Frost Group, Honig, and Brauser were all the subject to a lawsuit by the original founder of the company

The lawsuit by the original founder draws a clear link among Frost, Honig and Brauser, referring to them as the “Brauser Honig Frost Group,” with the following specific complaints from an article on the litigation:

“When BioZone Laboratories founder Daniel Fisher sold shares in his company to investors with Brauser Honig Frost Group, the parties entered a stock-sale agreement and an employment agreement that would provide Fisher with a job at the new BioZone Pharmaceuticals, according to court documents...

...His lawsuit also accuses Brauser Honig Frost Group and its investors, many of whom became executives at BioZone Pharmaceuticals after the sale, of violating the Racketeer Influenced and Corrupt Organizations Act for engaging in a pattern of similar behavior against other companies.

We describe [several] other suits against these defendants, either one or a group of them, in which a similar set of behaviors occurred,’ Darcy Paul [his lawyer] said. ‘This looks like a scheme.’”

Also, an investor would be forgiven for wondering why, in August 2013,92 BioZone sold convertible notes and warrants to MusclePharm, a company backed by Honig (including his company, GRQ Consultants) that lists Frost as a member of its “Scientific Advisory Board” (with MusclePharm leasing office space in Frost’s building).93,94 And then just last month it was announced that BioZone is going to sell “substantially all of [its] operating assets” to

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91 Based on 12/6/13 closing price of $0.64, stock has fallen 83% since its closing price of $3.69 (on 2/27/12)
92 See BioZone Q3 2013 10-Q (page 24)
93 See MusclePharm 2012 10-K (page 63)
94 See MusclePharm Q3 2013 10-Q Related Party Transactions (page 23)
MusclePharm. BioZone subsequently announced that it will merge with Cocrystal Discovery (a private company in which Opko and Frost are investors).

Opko is also involved with yet another investment with “the trio,” ChromaDex (CDXC). Opko made a $1 million investment in CDXC in February 2012 for a 1.5% ownership stake of the company. Once again, Opko is a shareholder alongside Frost (14.6% of the company), Honig (7.6% of the company) and Brauser (7.9% of the company). This time, Honig and Brauser are co-Chairmen of the company.

Here are some other connections that Frost has with Honig and/or Brauser that just further highlight the complicated web of relationships:

1. Castle Brands (ROX)
2. uSell.com (USEL)
3. Fuse Science (DROP)
4. Passport Potash (PPI CN)
5. SafeStitch Medical (SFES)
7. Data Acquisitions Group LLC (Private)
8. Bullfrog Gold (BFGC)
9. Silver Horn Mining (SILV)

Dr. Frost has also been involved in plenty of other penny stocks that do not (at least as far as we can tell) appear to have any Honig or Brauser involvement. Perhaps the most remarkable situation is that of Protalix BioTherapeutics (PLX). This company was merged with Orthodontix (traded on the pink sheets under OTIX) in August 2006. Simultaneously, Frost and Glenn Halpryn (who together owned a majority of Orthodontix) agreed to invest $15 million in Protalix. At that time, Frost and his trusted lieutenant, Dr. Jane Hsiao (who is the current Vice Chairman and Chief Technical Officer of Opko) joined the Protalix board. Interestingly, Eli Hurvitz was the Chairman of Protalix at the time and was also the Chairman of Teva at that point. Amazingly, on October 24, 2007, Protalix announced a 10 million share offering at $5 per share vs. the prior close of $36.06 per share, an astounding 86% discount. The next day, the stock fell 83%, “wiping away $2.07 billion in market value”. Dr. Frost and Hsiao, who had joined the board on 12/31/06, quit the Protalix board after the company’s implosion, with the press release citing “personal reasons.”

95 See Opko 9/30/13 10-Q (page 20)
Frost has also been involved with the following penny stocks:

1. Anfield Resources (ARY CN)
2. Non-Invasive Monitoring Systems (NIMU)
3. Tiger X Medical (CDOM)
4. Winston Pharmaceuticals (WPHM)
5. Alliqua (ALQAD)
6. Cadiz (CDZI)
7. Wright Investors’ Service Holdings (WISH)

If all this is not concerning enough, consider the following facts related to Opko’s former Chief Financial Officer. On July 16, 2012, long-time Frost colleague Rao Uppaluri retired from his role as CFO of Opko and was replaced by Juan Rodriguez. We find it strange that Uppaluri was listed as Treasurer and Director of Ideation Acquisition Corp, a publicly traded company, as recently as a 10-K filed on March 20, 2009 when at that same time, he was the CFO of Opko. But, Uppaluri’s bio in the Opko 10-K filed around the same time only discloses that he was on the board of Ideation (not that he was Treasurer). Also of note, at that time, Dr. Frost served as the Chairman of the Board for Ideation. Ideation ultimately merged with a company in China, changing its name to SearchMedia Holdings. SearchMedia was ultimately discovered to be a fraud, with its auditor KPMG resigning from the account and a lawsuit describing the fraud.

The complaint sums up the situation:

“Then on August 20, 2010, SearchMedia Holdings Limited announced that the historical financial statements of SearchMedia International Limited for the 2007 and 2008 fiscal years would have to be restated and that the financial statements from these periods should no longer be relied upon. SearchMedia Holdings Limited also indicated that it estimated that revenue in 2007 and 2008 had been overstated by approximately $6 million and $25 million, respectively. ...[the] stock fell nearly 23%, to close on August 20, 2010, at $2.62 per share. Over the next few days, SearchMedia’s stock continued to decline and closed at $1.70 per share on August 23, 2010, a 50% decline from the closing price of $3.40 per share on August 19, 2010.”

The company has since changed its name to Tiger Media (IDI) and trades for $1.30 per share with Frost still owning 28% of the company. Despite the fact that the company was a disastrous investment for Dr. Frost, that the books turned out to be fake and that the new Tiger Media (still

96 See Ideation 10-K (page 41)
97 See Opko 10-K (page 21)
trading under the ticker IDI), recorded no revenues for any of the past three years, Dr. Frost inexplicably continues to buy shares of this seemingly worthless entity with a ~$40 million market capitalization, most recently buying around $250,000 in stock on July 10, 2013.\(^9\)

The Tangled Web

K.) We Believe Insider Share Purchases At Opko Are A Red Herring

Dr. Frost has consistently purchased Opko shares in the open market and many investors seem to be buying the stock at any price based on this fact alone. The logic seems to go, "if Phil is buying, surely he must know something." Investors have been trained to follow insider buying, and we believe Dr. Frost has likely taken advantage of that fact to draw in many unsuspecting

\(^9\) See Tiger Media 2012 20-F (page F-4)
retail buyers that don’t fully understand what they own. We imagine Dr. Frost at this point realizes he is effectively “pot committed” in Opko and if he stops buying shares in the open market, confidence would likely disappear and the stock could plummet (his stake is also worth an astonishing $1.9 billion, which is a lot to fight hard to hold on to… not to mention what must be his keen interest in maintaining the support and trust of his followers).99

Consider this: Dr. Frost has engaged in insider purchases at Opko for years going back to 2007, and it is rather obvious now to us in hindsight that he didn’t “know something” after all, since everything the Company has been working on throughout that period has been a failure or disappointment (the Company’s main assets today were largely acquired just in the past year).

If Dr. Frost is buying the shares out of a genuine belief the shares are undervalued then why buy a little bit every day as opposed to all at once? Also, why would he go to such lengths to bolster the price through numerous television appearances and overly optimistic statements if he is trying to buy the stock for financial gain? To highlight what an unhealthy focus Opko has on its stock price, the Company issued a bizarre press release in February 2013 just minutes after the Company’s stock fell a few percent following the disclosure of a stock sale by the Chief Accounting Officer. The press release stated the sale was “done to address pressing family circumstances” and “no other sales by Company officers are currently contemplated.”

Perhaps even more importantly, shareholders might want to consider that for every share that Dr. Frost has purchased, the Company has issued nearly six more to finance acquisitions and raise capital over the years (fully-diluted shares have increased from 201 million in 2007 to 470 million today) – not the behavior we would expect from a company that believes its shares are a good value.

Finally, some Opko bulls have even put forth what we believe is the outlandish notion that Teva Pharmaceuticals might buy Opko given the connection to Dr. Frost. Consider that Teva’s market capitalization is $35 billion with $5.5 billion of operating profit vs. Opko’s market capitalization of $5 billion with run-rate losses of $100 million… how can a public company Board of Directors ever consider such a transaction? We would like to point out that based on the Opko/Prolor merger proxy, it appears Teva conducted due diligence and passed on a deal to buy Prolor (and that would be one-tenth the size of Opko). And lastly, consider everything included in this report and imagine a public company board ever considering spending $5 billion or more on this company.

99 Based on an estimated 172.8mm diluted shares beneficially owned by Frost, The Frost Group, LLC and Frost Gamma Investments Trust, pro forma for the Prolor acquisition and including all warrants, options and convertible debt based on the treasury method; based on latest 13D plus subsequent open market share purchases
**L.) Analyst Coverage is Biased and Perennially Incorrect**

The only significant sell-side research firms that cover Opko’s stock include Ladenburg Thalmann, which is Dr. Frost’s company, and Jefferies, which is the Company’s underwriter and M&A advisor. Not surprisingly, both firms have consistently been way too bullish on Opko’s prospects.

In Ladenburg’s July 14, 2011 initiation report, the analyst claimed:

> “The market for an effective blood-based Alzheimer’s screening test could approach $3B annually...
>
> Our model calls for OPK to become cash flow positive by 2014 based on introduction of the Alzheimer’s diagnostic test (launch in 2013) and potential contribution from the vaccine franchise. If OPK is successful in launching its Alzheimer’s test, in our view, the company may not need additional capital to finance development of its current pipeline.”

It is now fairly obvious that Opko will almost assuredly be significantly cash flow negative in 2014, the Alzheimer’s test did not launch in 2013 and appears to be a failure and the Company has already raised capital through a $175 million convertible debt issuance (not to mention the considerable stock issuance for acquisitions).

A March 7, 2013 Ladenburg note highlighted that Opko’s asset sale agreement with RXi Pharmaceuticals (RXII) for certain intellectual property for RXi stock valued at $7 million (plus milestones and royalties) “unlocks significant long term value.” It is unclear to us how such an immaterial transaction to a $5 billion company is even worthy of mention, much less an argument that it “unlocks value.” In any case, these programs are unlikely to be worth anything in the hands of RXi (with a market capitalization below $40 million), as even Ladenburg admits that this IP relates to programs that “previously failed to meet a futility analysis in Phase III.”

Then on March 19, 2013 (just twelve days after the prior note), Ladenburg released yet another note in which they explained that “OPK reiterated plans to launch the Claros point-of-care PSA test during 2H13 in Europe and to submit a 510(k) to FDA in 2014.” While the 10-K does not comment on timing of [a] U.S. launch for 4KScore™, we continue to expect the test to be introduced in [the] U.S. during 2013.” Again, Opko failed to deliver on each of the 2013 goals but was again not held accountable by the analyst community.

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100 Ladenburg Thalmann report dated July 14, 2011: *Putting Together the Pieces: 3 Potential Best in Class Assets Lay the Foundation for Sustainable Growth. Initiating Coverage with Buy Rating and $6.00 PT*


After helping complete a March 2011 equity offering as the lead bookrunner, Jefferies initiated coverage of Opko on November 10, 2011 with a Buy rating and an $8 price target. In the report, the analyst stated that “With the recent Claros acquisition, OPK is to launch Claros’ point-of-care PSA system in Europe in 1Q12; with potential 510(k) approval in the U.S. by YE12, we forecast ~$500M in peak U.S./EU sales.” As we have discussed, neither of these dates were met and Claros has not generated a single dollar of revenue. In her sum of the parts, the Jefferies analyst even assigns a value of “~$3/sh for Claros’ PSA system.” To highlight the absurd nature of this valuation, at that time, Opko had roughly 330 million diluted shares outstanding, so she was valuing Claros at almost $1 billion even though it had been acquired just the previous month in a competitive auction for $30 million.

The same report stated that the test for “for Alzheimer’s disease (AD) and cancers (yet-to-be proven technology) could provide significant long-term upside potential (>~$800M in sales).” Again, this program has been an apparent failure and has generated zero revenues for Opko.

In an April 19, 2012 report, Jefferies acknowledged that there had been “delays in some of the programs” and went on to highlight “…(1) results from diagnostic validation study for Alzheimer’s disease now expected in ~2H12 (vs. 1Q12 previously), (2) EU launch of Claros’ point-of-care PSA system now expected in 2H12 (vs. 1Q12 previously) and (3) data from 6-month study for Claros’ point-of-care PSA system … in ~2013 (vs. 2H12 previously).” Yet amazingly none of these disappointments or delays resulted in any change to the price target despite a 32% reduction in estimated 2014 revenues vs. her initiation report. And in any event, Opko subsequently missed each one of these new, later deadlines.

In a May 13, 2013 report, the Jefferies analyst excitedly discussed the “4Kscore™ U.S. launch in ~mid-2013 in [a] non-Medicare patient population by Prost-Data (CLIA-certified lab) using ~30 sales reps.” Yet three months later, with no change to her price target, the expected timing was quietly dropped in an August 12, 2013 report, where she described the timing as “…4Kscore™ U.S. launch in [a] non-Medicare patient population by Prost-Data (CLIA-certified lab) using ~30 sales reps (timing undisclosed).”

In the most recent report dated November 12, 2013, Jefferies conceded that “With delays in Dx development/launches (e.g., 4Kscore™, Claros-1 system for prostate cancer), OPK’s focus is now on pharmaceuticals…” Yet oddly, these developments warranted a price target increase to $11.50 per share.

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104 See Opko 9/30/11 10-Q (page 26)
105 Jefferies report dated April 19, 2012: Financial Update; Validation Study Data for AD Dx in ~2H12
106 2014 revenues of $57.6mm in report on 4/19/12 vs $85.3mm on 11/10/11, a decrease of 32%
107 Jefferies report dated May 13, 2013: Wider 1Q13 Net Loss
108 Jefferies report dated August 12, 2013: Update of 2Q13 Financial Results; Prolor Acquisition to Close in 3Q13
109 Jefferies report dated November 12, 2013: Wider 3Q13 Net Loss; Ph3 Data for TSRO’s Rolapitant by YE13
M.) We Believe Opko Shares Are Worth 75% to 100% Less Than The Current Price

Based on our research as detailed in this report, it is our belief that Opko will never generate a profit, which would render an ultimate share price of $0 per share. Even under an incredibly optimistic scenario whereby the 4Kscore™, Cytochroma and Prolor Biotech were each worth $500 million and all other assets generated enough money to cover operating losses (thereby netting to a value of zero), the stock would only be worth $3 per share, or nearly 75% below the current price.

### Opko Valuation Summary

<table>
<thead>
<tr>
<th></th>
<th>$ Millions</th>
<th>$ Per Diluted Share</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
<td><strong>High</strong></td>
<td><strong>Low</strong></td>
<td><strong>High</strong></td>
</tr>
<tr>
<td>Drug Distribution</td>
<td>$0 - $30</td>
<td>$0.00 - $0.06</td>
<td>$10mm in 2012 gross profit</td>
</tr>
<tr>
<td>Alzheimer's Test</td>
<td>0 - 0</td>
<td>0.00 - 0.00</td>
<td>Apparent failure as discussed above</td>
</tr>
<tr>
<td>Claros Diagnostics</td>
<td>0 - 50</td>
<td>0.00 - 0.11</td>
<td>Significantly delayed; purchased for $30mm</td>
</tr>
<tr>
<td>4Kscore™</td>
<td>0 - 500</td>
<td>0.00 - 1.06</td>
<td>Significantly delayed; no upfront payment to acquire</td>
</tr>
<tr>
<td>Rayaldy / Cytochroma</td>
<td>0 - 500</td>
<td>0.00 - 1.06</td>
<td>Acquired for $100mm earlier this year</td>
</tr>
<tr>
<td>Prolor Biotech</td>
<td>222 - 500</td>
<td>0.47 - 1.06</td>
<td>Oppenheimer valuation of $222-$284mm; Opko acquired for $480mm</td>
</tr>
<tr>
<td>Other (Rolapitant, Farmadiet, etc)</td>
<td>0 - 250</td>
<td>0.00 - 0.53</td>
<td></td>
</tr>
<tr>
<td>Overhead (excluding above programs)</td>
<td>(350) - (550)</td>
<td>(0.74) - (1.17)</td>
<td>$35-$55mm in annual burn at 10x</td>
</tr>
<tr>
<td>Projected Net Cash at 12/31/13</td>
<td>146 - 146</td>
<td>0.31 - 0.31</td>
<td>Excludes convertible debt balance (reflected in diluted share count)</td>
</tr>
<tr>
<td><strong>Opko Equity Value</strong></td>
<td>$17 - $1,426</td>
<td>$0.04 - $3.03</td>
<td></td>
</tr>
<tr>
<td><strong>% Above/(Below) Current Share Price</strong></td>
<td>(100%) - (73%)</td>
<td></td>
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</table>

We believe we may be reaching the point at which Opko’s shares begin trading in-line with a reasonable estimate of fair value. We believe the combination of Dr. Frost’s buying, intense retail buying and unrealistically bullish analyst research was able to have an outsized impact on Opko’s stock price historically when its free float was small, but now with the current free float having more than tripled in value over the past year, we believe it is much more likely that Opko’s shares will reflect reality in the future.

We estimate the free float of Opko has expanded from $650 million one year ago to $2.5 billion today due to (1) the all-stock acquisitions of Cytochroma, Prost-Data and Prolor Biotech, (2) the partial early conversion of the convertible debt into equity and (3) the sharp rise in the share price.
9/30/12 Fully-Diluted Shares Outstanding 336 million
Less: Shares Owned by Dr. Frost - 132 million
Less: Shares Owned by Other Insiders (Hsiao, Rubin, etc.) - 30 million
Less: Shares to be Issued for Convertible Note - 0 million
Less: Options and Warrants Outstanding (via Treasury Method) - 26 million

9/30/12 Number of Shares in Free Float 148 million
Multiplied by: Opko Share Price (11/30/12) x $4.38 per share

9/30/12 Opko Free Float ($) $648 million

9/30/13 Fully-Diluted Shares Outstanding 470 million
Less: Shares Owned by Dr. Frost - 156 million
Less: Shares Owned by Other Insiders (Hsiao, Rubin, etc.) - 32 million
Less: Shares to be Issued for Convertible Note - 22 million
Less: Options and Warrants Outstanding (via Treasury Method) - 39 million

9/30/13 Number of Shares in Free Float 221 million
Multiplied by: Opko Share Price (12/9/13) x $11.10 per share

9/30/13 Opko Free Float ($) $2.5 billion

Furthermore, the stock has been added to the TASE 25 index (Tel Aviv) and saw its weighting in the Russell 2000 increase at the end of August, which in turn have increased the shares that are available for borrow (as index funds generally lend out their shares). As a result, Opko shares can now be borrowed by short sellers at a current annual rate of <10% whereas they were nearly impossible to borrow over the course of the past year.

N.) Conclusion

We believe Opko shares offer little in the way of substance and a great deal in the way of illusion. We believe Opko shareholders have unknowingly been fed a placebo, a mere sugar pill of insider share purchases, overhyped opportunities and bullish analyst forecasts. The problem, of course, with a placebo is generally one of confidence. As long as people believe in the efficacy of a placebo, it has remarkable powers, but once people realize this supposed wonder drug is just a simple sugar pill, its powers can suddenly disappear.
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