GLAUCUS RESEARCH GROUP

"The art of medicine consists in amusing the patient while nature cures the disease." - **Voltaire**

THIS RESEARCH REPORT EXPRESSES OUR OPINIONS. Use Glaucus Research Group California, LLC's research opinions at your own risk. This is not investment advice nor should it be construed as such. You should do your own research and due diligence before making any investment decisions with respect to the securities covered herein. We are short Tekmira and therefore stand to realize significant gains in the event that the price of Tekmira's stock declines. Please refer to our full disclaimer located on the last page of this report.

COMPANY: Tekmira Pharmaceuticals Corp. | Nasdaq: TKMR
INDUSTRY: Biotechnology

Recommendation:
Strong Sell

Price:
$16.75
As of Close 11/7/2014

Market Cap:
$370mm

Daily Volume
5.3mm shares
(Avg. 3mo)

Price Target:
$7-10

Tekmira Pharmaceuticals Corp (NASDAQ: TKMR) ("Tekmira" or the "Company") is a Vancouver-based biopharmaceutical company focused on developing RNA-interference ("RNAi") delivery technology using the Company's proprietary lipid nanoparticle ("LNP") delivery platform. In the last three months, Tekmira's share price has nearly doubled because the U.S. Food and Drug Administration ("FDA") temporarily lifted a clinical hold on the Company's anti-Ebola RNAi therapeutic ("TKM Ebola") to allow the drug's administration to Ebola infected patients in emergency situations.

Tekmira is hugely overvalued and its share price is poised to collapse. Tekmira's RNAi technology is unproven, the FDA halted TKM Ebola's Phase I trial because of safety concerns, and despite limited use it appears that the drug is unpopular among treating physicians. In our view, the drug is highly likely to fail the FDA approval process. Once the speculative bubble bursts, we believe that Tekmira's shares will crash to a pre-Ebola price of $7-10 per share.

1. **Dose of Reality.** In July 2014, the FDA placed a clinical hold on Phase I trials of TKM Ebola, reportedly because of elevated cytokine levels among healthy volunteers (which at higher levels can prompt dangerous inflammation and other negative responses from the immune system). A failure at this stage over safety concerns makes it highly unlikely the drug will ever be approved.

    a. **Doctors Fear that TKM Ebola is Toxic and Unsafe**. Temporary approval for emergency administration does not change the fact that the FDA halted Phase I trials because of TKM Ebola's safety risks and potential toxicity. Indeed, experts have cautioned that treating physicians may be reluctant to administer TKM Ebola because of the perceived risk: "they may want to use a drug with the cleanest safety profile. **You may not want to give him a drug that will push [patients] over the edge**." Put simply, TKM Ebola has not been shown to be either safe or effective and its limited use in the current crisis does not increase the likelihood of approval by the FDA.

    b. **Treating Physicians Seem to Prefer Other Experimental Treatments**. To our knowledge, TKM Ebola was only administered **after supplies of** a competitive treatment, ZMapp, were exhausted. TKM Ebola has only been administered to two patients (one in Nebraska, one in Norway) and the hospital in the US which first administered TKM Ebola chose a competitor's drug, Brincidofovir, to treat a subsequent patient. It appears that treating physicians clearly favor blood transfusions from survivors, Brincidofovir and especially ZMapp over TKM Ebola.

2. **Partners Know Best: Declining Interest in Licensing or Partnering with Tekmira**. Pharmaceutical companies who have signed licensing, collaboration or partnership deals with Tekmira appear unlikely to renew such arrangements and seem uninterested in pursuing further commercial relationships. Specifically, Roche, Alnylam and Bristol Myers Squibb all signed deals with Tekmira at the height of RNAi excitement in 2008-2009, and subsequently each one either terminated this collaboration (Roche, Alnylam) or seem uninterested in increasing a paltry commercial commitment (BSM). It therefore appears that developers and other insiders do not assign Tekmira's technology a high probability of commercial success.

3. **Impractical Delivery Mechanism**. TKM Ebola is wildly impractical for distribution in Ebola target zones (Sub-Saharan Africa) because it is administered **intravenously**, which requires trained medical personnel and resources. This makes TKM Ebola's widespread commercial use unlikely in Sub Saharan African regions that could not contain the spread of Ebola because they lacked trained medical professionals and such basic resources as masks, gowns and gloves.

4. **Tekmira's RNAi Technology is Unproven**. Since Andrew Fire and Craig Mello's groundbreaking 1998 paper, **not a single RNAi compound has been successfully approved by the FDA for clinical development**. The technology has fallen into such disfavor that Merck, Roche, Pfizer and Abbott appear to have divested or abandoned their respective in-house RNAi research efforts.

5. **Valuation**. We believe that Tekmira is hugely overvalued and that its share price is poised to collapse. RNAi technology is unproven, TKM Ebola's Phase I trial was halted over safety concerns, and nothing since, including limited application to two patients under exigent circumstances makes it any more likely that TKM Ebola is safe, efficacious and thus likely to gain FDA approval. In addition, there is evidence that treating physicians prefer other experimental treatments, and it appears that presumably due to concerns over TKM Ebola's safety risks, Tekmira's Ebola therapeutic is an experimental treatment of last resort. We therefore believe that Tekmira should be valued at its pre-Ebola valuation, between $7-10 per share.

DOSE OF REALITY FOR TKM EBOLA

In August 2014, the FDA's decision to allow the administration of experimental treatments, including TKM Ebola, under emergency circumstances prompted an 80% jump in the price of Tekmira's shares in just four trading days. But it is critical to note that the use of TKM Ebola in exigent circumstances does not increase the likelihood that the therapeutic will receive FDA approval or in any way undermine the primary detractions of Tekmira's technology, including credible concerns about the safety and toxicity of the treatment.

1) Doctors Fear that TKM Ebola is Toxic and Unsafe

The purpose of Phase I of clinical trials is to test a new drug in a small group of volunteers to evaluate its **safety** and identify any side effects. 60-65% of prospective drugs pass Phase I clinical trials, so a setback at this stage over safety and potential toxicity concerns makes it highly unlikely that a prospective drug will ever be approved.

In January 2010, Tekmira reported that it had prematurely terminated a Phase I clinical study of TKM-ApoB (the first clinical candidate to employ Tekmira's proprietary LNP delivery platform) due to immune stimulations observed *in healthy patients* at moderate doses (0.6mg/kg). This result did not come as a surprise to many industry insiders. Indeed, one executive in the RNAi space who had been involved in a collaboration with Tekmira, admitted with respect to the Company's LNP delivery technology that "**the liability of the platform is absolutely its safety**."[1]

In response, Tekmira purportedly addressed potency issues and was set to re-test the tolerability of its proprietary LNP delivery platform.[2] Tekmira got its chance, and on March 5, 2014, the Company received Fast Track designation from the FDA for Phase I clinical trials of TKM Ebola. It did not go well.

In July 2014, Tekmira received a notice that the FDA had placed TKM-Ebola's Phase I trial on a clinical hold because of elevated cytokine levels observed in healthy volunteers. Cytokine release can spur deadly fevers in patients and cause negative responses from the immune system.[3] Under the FDA's CFR Title 21, the FDA can put Phase I investigations on clinical hold if it believes that "human subjects would be exposed to an unreasonable and significant risk of injury."

This prompted a sell-off in the stock, both because of the apparent failure of the TKM Ebola but also because of the implications of the clinical hold for TKM's other therapeutics, principally TKM-HBV. TKM Ebola generated side effects which could make patients feel worse at the onset of treatment, which could deter its administration to very sick patients (many Ebola patients are, unsurprisingly, very sick when they finally seek treatment, especially in Africa).

One month later, in August 2014, the Ebola situation in West Africa worsened and the first person died from the disease in Western Europe. This prompted the FDA to modify its clinical hold on TKM Ebola to a partial hold, meaning that TKM Ebola could be administered in emergency situations to infected patients. However, the FDA cautioned that the study "[remains] on clinical hold as it relates to the multi-ascending dose portion of the Phase I clinical study in healthy volunteers with TKM Ebola."

[1] http://www.xconomy.com/national/2010/01/21/mercks-alan-sachs-on-rnais-big-challenge-delivery-delivery-delivery/?single_page=true
[2] http://rnaitherapeutics.blogspot.com/search/label/Tekmira
[3] http://www.fiercebiotech.com/story/sarepta-leaps-ebola-spotlight-shelved-therapy/2014-08-06

Investors do not appear to have heeded such caution. Tekmira's stock skyrocketed almost as quickly as stupidity regarding Ebola proliferated. Jason Kolbert of Maxim (which, unsurprisingly, was a co-manager on Tekmira's October 2013 round of capital raising) reportedly raised his price target from $23 to $31 due to accelerated assumptions for TKM Ebola.

2) Treating Physician Prefer Other Experimental Treatments

Seemingly forgotten in Tekmira's stock bubble is that TKM Ebola was administered to treat patients **only** after the supply of the preferred experimental therapy, ZMapp was exhausted.

Following the partial lift, TKM Ebola was administered to Dr. Richard Sacra, an American who was flown back to Nebraska Medical Center from Liberia for treatment. He survived. Tekmira's stock soared in response, despite the fact that Dr. Sacra also received other treatments (in addition to TKM Ebola) and there was no conclusive evidence that Tekmira's therapeutic had any effect on the patient's recovery.

Indeed, Dr. Angela Hewett, associate medical director of the Nebraska Medical Center's bio-containment unit, cautioned that it was unclear if TKM Ebola was effective: "we don't know if it was Dr. Sacra's own immune system, the supportive therapy we provided, the blood transfusion from Dr. Brantly, TKM Ebola or a combination of all these factors that helped Dr. Sacra recover."

Then the bad news for Tekmira started rolling in. On October 6th, at the request of treating physicians, the FDA approved Brincidofovir, a drug offered by Chimerix, for administration to Ebola patients. On October 7th, Nebraska Medical Center disclosed that it would administer Brincidofovir, not TKM Ebola, to NBC cameraman Ashoka Mukpo. Nebraska Medical Center was the only hospital in the U.S. (to our knowledge) to administer TKM Ebola, so many investors took its decision to administer Brincidofovir to Mukpo as a tacit rejection of TKM Ebola.

On October 9th, a panel of WHO experts said that after reviewing the status of all the potential experimental therapies and vaccines, blood plasma and whole blood transfusions should have priority for the time being. Indeed, three Ebola patients who received a blood transfusion from Dr. Brantly, including Mukpo, Sacra and Nina Pham, have survived.

To our knowledge, TKM Ebola has not been administered in the United States since it was used to treat Dr. Sacra.

We have compiled, based on our review of the publicly available disclosures, a table setting forth the various treatments administered in North America and Europe to patients infected with Ebola. Although this list is not dispositive, we believe it is indicative in that it shows that the preferred treatments appear to be ZMapp and blood transfusions from surviving patients.

Patient Usage - As of 11/9/14

Name of Patient	Occupation	Arrival/Admitted Date	City/Country	Hospital	Status	Experimental Drug Treatment?	TKM-EBOLA	Blood/Plasma Transfusion	ZMAPP	Chimerix Brincidofovir	Toyama Chemical (Fujifilm) Favipiravir	Other
US PATIENTS												
Dr. Kent Brantly	Missionary	Aug 2nd	Atlanta, GA	Emory University Hospital - Atlanta	Recovered	Yes		X	X			
Nancy Writebol	Aid Worker	Aug 2nd	Atlanta, GA	Emory University Hospital - Atlanta	Recovered	Yes			X			
Dr. Richard Sacra	Doctor	Sept 5th	Omaha, NE	Omaha - Nebraska Medical Center	Recovered	Yes	X	X		X		
Unknown Male WHO Doctor	Doctor	Sept 9th	Atlanta, GA	Emory University Hospital - Atlanta	Recovered	Unclear						
Thomas Eric Duncan	Visitor	Sept 30th	Dallas, TX	Texas Health Presbyterian Hospital	Died	Yes				X		
Ashoka Mukpo	NBC Cameraman	Oct 6th	Omaha, NE	Omaha - Nebraska Medical Center	Recovered	Yes		X		X		
Amber Jay Vinson	Hospital Worker	Oct 15th	Atlanta, GA	Emory University Hospital - Atlanta	Recovered	No						
Nina Pham	Hospital Worker	Oct 16th	Bethesda, MD	National Institutes of Health (NIH)	Recovered	No		X				
Craig Spencer	Doctor	Oct 23rd	New York, NY	Bellevue Hospital Center	In Treatment	Yes		X		X		
EUROPEAN PATIENTS												
Name of Patient	**Occupation**	**Arrival/Admitted Date**	**City/Country**	**Hospital**	**Status**	**Experimental Drug Treatment?**	**TKM-EBOLA**	**Blood/Plasma Transfusion**	**ZMAPP**	**Chimerix Brincidofovir**	**Toyama Chemical (Fujifilm) Favipiravir**	**Other**
Miguel Pajares	Missionary	Aug 7th	Madrid, SP	Carlos III Hospital	Died	Yes			X			
Will Pooley	Nurse	Aug 24th	London, UK	Royal Free Hospital	Recovered	Yes			X			
Undisclosed	Doctor	Aug 27th	Hamburg, Germany	University Medical Center Hamburg-Eppendorf	Recovered	No						
Undisclosed	Nurse	Sept 19th	Paris, FR	Military Hospital	Recovered	Yes					X	
Manuel Garcia Viejo	Priest	Sept 22nd	Madrid, SP	Carlos III Hospital	Died	Unclear						
Undisclosed	Doctor	Oct 3rd	Frankfurt, Germany	University Hospital	Recovered	Yes					X	Hemopurifier by Aethlon medical; FX06
Teresa Romero	Nurse	Oct 6th	Madrid, SP	Carlos III Hospital	Recovered	Yes			X			
Undisclosed	U.N. Medical Worker	Oct 6th	Leipzig, Germany	St. Georg Clinic	Died	Yes						FX06
Silje Michalsen	Aid Worker	Oct 6th	Oslo, Norway	Ullevål hospital	Recovered	Yes	X		X		X	

As shown above, it appears that treating physicians have preferred blood transfusions and the drugs of Tekmira's competitors (ZMapp and Brincidofovir) to TKM Ebola. We could only find two instances were treating physicians administered TKM Ebola. In each case, it appears that the treating hospital accompanied the administration of TKM Ebola with the administration of a competitor's experimental treatment (ZMapp or Brincidofovir). This makes it appear as though TKM Ebola is a treatment of last resort.

Even the Center for Disease Control ("CDC") appears to favor ZMapp as the preferred treatment. The CDC's webpage dedicated to experimental Ebola treatments discusses ZMapp and its application and availability for the first 10 paragraphs, whereas TKM Ebola only receives passing mention by the CDC in one paragraph at the bottom of the page.

Admittedly, the sample size is tiny and investors should be wary of drawing conclusions. But to our knowledge, the only hospital in the United States to administer TKM Ebola preferred the drug offered by its competitor to treat a future patient.

As noted by University of Pittsburgh Medical Center specialist for infectious disease, Amesh Adalja, treating physicians may be reluctant to administer TKM Ebola because of the perceived safety risk: "they may want to use a drug with the cleanest safety profile. **You may not want to give him a drug that will push him over the edge**." TKM Ebola's risk profile suggests that despite its temporary approval for emergency use, investors should not be pricing into its stock price a high likelihood that it will widely adopted as a treatment or that such limited application increases the likelihood of FDA approval.

CUSTOMERS KNOW BEST: DECLINING INTEREST IN TEKMIRA

We admit that it is difficult to predict whether experimental treatments will succeed. But we trust that those closest to Tekmira's technology know best. And it appears as though Tekmira's customers and former collaborators assign the technology a low probability of success.

1) Customer Churn

Investors should be worried that customers who signed licensing or partnering deals with Tekmira appear unlikely to either pursue further commercial relationships or augment small commercial commitments.

During the peak of the RNAi bubble (2005-2009), several major pharmaceutical companies signed licensing and collaboration deals with Tekmira to develop applications for the Company's LNP delivery platform. However, it is evident from the chart below that many such partners have since become disinterested in further collaboration.

Hibiki Historical Revenue*

Figures are in US$mm	1H2014	2013	2012	2011	2010	2009	2008
Alnylam	-	-	-	4.2	6.3	8.8	6.1
U.S. Government	$ 4.10	9.8	11.5	11.5	3.6	-	-
Roche	-	-	-	-	4.5	4.8	0.2
Bristol-Myers Squibb Company ('BMS')	0.21	0.5	0.4	0.4	0.2	0.2	0.4
Other RNAi collaborators	-	0.1	0.1	0.1	0.4	-	0.1
Total collaborations and contracts	**4.83**	**10.4**	**12.1**	**16.3**	**14.9**	**13.8**	**6.6**
Alnylam milestone payments	-	5.0	1.0	0.5	0.5	0.6	5.1
Monsanto Licensing fees and milestone payments	1.17	-	-	-	-	-	-
Other (Acuitas and Spectrum)	0.24	-	1.0	-	-	-	-
Talon license amendment payment	-	-	-	-	5.9	-	-
Total Licensing Fees, milestones, and royalty payments	**1.41**	**5.0**	**2.0**	**0.5**	**6.4**	**0.6**	**5.1**
Total revenue	**$ 6.24**	**15.5**	**14.1**	**16.8**	**21.4**	**14.4**	**11.7**

Deferred collaborations and contracts revenue as of June 30, 2014**

Collaborators and Partners	**US$mm**
DoD	**$ 0.311**
Monsanto current portion	**4.143**
BMS	**1.589**
Deferred revenue, current portion	**6.043**
Monsanto long-term portion	**10.510**
Total deferred revenue	**$16.553**

source:

*2010 20-F: http://www.sec.gov/Archives/edgar/data/1447028/000119312511158553/d20f.htm

*2013 10-K : http://www.sec.gov/Archives/edgar/data/1447028/000117184314001457/f10k_032714.htm

*2Q'1410-Q - http://www.sec.gov/Archives/edgar/data/1447028/000117184314003980/f10q_081314.htm

**2Q'1410-Q - http://www.sec.gov/Archives/edgar/data/1447028/000117184314003980/f10q_081314.htm

In the irrational exuberance of 2009, Tekmira partnered with Roche and Alnylam for a Phase I clinical trial of a therapeutic for hypercholesterolemia.[4] But Roche terminated the relationship following the premature termination of Tekmira's first clinical trial of its LNP delivery technology in 2010, and Roche subsequently exited the entire RNAi space by selling its Wisconsin-based RNAi research assets to another competitor, Arrowhead Research.[5]

Bristol-Myers Squibb, despite paying a few hundred thousand dollars per year to Tekmira, has so far refrained from increasing the scale of its *de minimis* financial commitment.

By far Tekmira's most significant collaborator, customer and partner since inception has been Alnylam. Some biotech commentators have described the relationship of the companies as an 8-year "marriage." Alnylam was historically Tekmira's largest customer, accounting for $38mm (over 40%) of Tekmira's revenues from 2008-2013. Following an acrimonious split, Tekmira sued Alnylam in 2011 for misappropriation of its RNAi intellectual property.

In November 2012, Alnylam and Tekmira settled its on-going dispute, with Alnylam agreeing to pay Tekmira $65 million up front. In exchange, Alnylam won the right to terminate its manufacturing agreement with Tekmira and amend a license to use Tekmira's technology which had the effect of lowering the royalty and milestone payments to which Tekmira would be entitled in the event Alnylam's therapeutic was successful.

As evidenced by Alnylam's current portfolio,[6] Alnylam has made the conscious decision to terminate its relationship with Tekmira and develop its own proprietary LNP delivery platform, eliminating Alnylam's reliance on Tekmira for the development of future therapeutics.[7]

Although it is notoriously difficult to evaluate the prospects of complex biotechnology such as the LNP delivery platform marketed by Tekmira, there are short cuts. It appears that larger pharmaceutical companies who sign collaboration deals with Tekmira either terminate such relationships (Roche, Alnylam) or are not sufficiently impressed to increase a tiny financial commitment (BSM).

Tekmira's former collaborators and partners had a clear financial incentive to participate in the development of a successful technology and a greater knowledge of the probability of such success than any investor. Investors could therefore infer that because such firms have all chosen to either terminate (or at the very least not expand) initial commitments to the Company, it would seem that industry experts do not assign Tekmira's technology a high probability of commercial success.

2) Department of Defense

As of April 2014, Ebola had killed 1,700 people and infected only 2,500 since 1976. The number of deaths has risen to roughly 10,000 (total) with the latest outbreak, with almost all of the fatalities limited to Sub-Saharan Africa. Given that experts admit that it is highly unlikely for Ebola spread in the United States or Europe, the commercial viability of Ebola drugs is thus limited. Based on the impracticalities of TKM Ebola's distribution mechanism (IV bags), in all likelihood the only customer for an approved TKM Ebola therapeutic is the U.S. government.

[4] http://www.sciencemag.org/site/products/lst_20091016.xhtml
[5] http://www.arrowheadresearch.com/press-releases/arrowhead-research-corporation-acquires-roche-rna-assets-and-site
[6] From a July 22, 2014 ALNY roundtable presentation, Slide 7
[7] For those interested in the nuances of ALNYs technology feel free to reference:
http://www.alnylam.com/web/assets/Roundtable_ESC-GalNAc-Conjugates_072214.pdf

In 2010, Tekmira announced a $140 million contract with the Department of Defense (the "DoD") to utilize its LNP technology in development of an Ebola treatment. In 2013, Tekmira claimed that this collaboration was "expanded" to incorporate new LNP technology.

Although this contract has been Tekmira's primary source of revenue since 2010, there is good reason to believe that this collaboration is not the coup that Tekmira claims it to be.

First, it is misleading to characterize Tekmira's collaboration with the DoD as a '$140' million contract. Under the terms of the agreement, Tekmira was eligible to receive $34.7 million from 2010 through 2013. Thereafter, the DoD has an annual option to extend the contract. If the DoD keeps extending the contract, the DoD has the authority but not the obligation to allocate up to $140 million towards TKM Ebola. Just because the program gives the DoD the discretion to spend up to $140 million does not mean that Tekmira won a $140 million contract – at least not in the way that most investors, layman and bartenders think about contracts.

The DoD chose to extend the contract (we believe on an annual basis) in both 2013 and 2014, but there is absolutely no guarantee that it will spend the remainder of the eligible amount on TKM Ebola. The risk of early termination is real. At the end of 2012, DoD threatened to cut the funding for TKM Ebola. Ultimately, it decided to continue, but continuing DoD commitment is by no means a certainty.

Second, the government is also backing Tekmira's competitors. The DoD Threat Reduction Agency also provides funding for the development of ZMapp, BioCryst's Brincidofovir,[8] and a vaccine developed by Newlink. Investors should not be fooled by Tekmira's press releases, which seem to imply that the DoD has picked a winner in a crowded Ebola treatment field.

[8] http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/qa-experimental-treatments.html

DELIVERY MECHANISM FOR TKM EBOLA COMMERCIALLY IMPRACTICAL

Even if, in the unlikeliest of scenarios, TKM Ebola is approved for clinical development by the FDA, its adoption may be limited because its delivery mechanism is wildly impractical for distribution and use in Ebola target zones. This limits the drug's commercial viability and by extension, should temper the best-case-scenario upside predicted by many Tekmira proponents.

TKM Ebola is administered intravenously. This presents a challenge in sub-Saharan African regions most at risk for Ebola outbreaks. Such regions are underserved and characterized by the absence of remotely adequate medical infrastructure.

Ebola has spread in countries such as Guinea, Sierra Leone, Liberia, the Central African Republic, and the Democratic Republic of Congo who have few medical professionals and even fewer basic resources like gloves, masks and gowns, which are critical in protecting health care workers from infection.

How likely is it that a facility without gloves, gowns and masks will have the resources and expertise to intravenously administer an IV therapeutic? Administration of TKM Ebola requires careful dosage calibration from a trained professional. In addition, the FDA has warned of a shortage of saline IV bags, meaning such bags will be even harder to obtain in Sub-Saharan Africa.

Because of limited resources and medical expertise in Ebola-heavy regions of Sub-Saharan Africa, TKM Ebola's IV delivery mechanism makes it unlikely to garner widespread adoption in the very part of the world it would be most likely to be administered.

By contrast, Tekmira's principal competitive threats other than ZMapp (Chimerix, Toyama and Biocryst) have delivery mechanisms much more suited to treating Ebola in Sub-Saharan Africa, where it matters most. Chimerex's Brincidofovir is an oral pill which can be stored at room temperature, making it far more desirable not only for manufacturing but also for delivery and administration to at-risk areas in sub-Saharan Africa.

Drug Treatment and Therapy Administration Comparison

Company	Drug Name	Treatment Administration
Tekmira	TKM-Ebola	Bolus IV Infusion
Sarepta	AVI-7537	Bolus IV Infusion
Mapp Boipharmaceutical	ZMAPP	Bolus IV Infusion
Chimerix	Brincidofovir	Oral Pill
Toyama Chemical	Favipiravir (or T-705)	Oral Pill
Biocryst	BCX4430	Intramuscular (IM) Injection

The impracticality of administering TKM Ebola in regions lacking experienced medical personnel and basic resources undermines the commercial viability of the drug. This is relevant to Tekmira investors because the Company's current valuation implies both a statistical likelihood that TKM Ebola will be an approved and useful treatment for Ebola (an outcome that we consider entirely remote) but in the event of such approval, that TKM Ebola will be a widely disseminated and adopted technology to treat the disease. We think not.

RNAi TECHNOLOGY UNPROVEN

Most drugs fail. A recent study published in *Nature Biotechnology* reported that the probability of FDA approval for drugs in Phase 1 of development was between 10-15%.[9] Such a success rate would be the envy of RNAi biotechnology firms. To date, not a single RNAi compound has successfully completed the FDA approval process to clinical development, despite billions in investment into the commercial application of RNAi therapeutics. Tekmira's RNAi based Ebola treatment is based on technology that is not only unproven, but has proved an overhyped wasteland of pharmaceutical investment since inception.

DNA carries the genetic information of a cell, consisting of thousands of genes. To create proteins, such genetic information is first transcribed into messenger RNA. Once mRNA is transported outside the nucleus of a cell, the code in the RNA is translated into a protein.[10]

RNA interference ("RNAi") is a posttranscriptional process of regulating specific genes using small fragments of nucleic acid. In theory, small molecules could be synthesized to inhibit the expression of proteins by causing the degradation (or inhibition) of specific messenger RNA molecules,[11] preventing their translation.[12] The promise of RNAi therapeutics is to attack the problem at its source by eliminating the creation of the very proteins that cause disease.[13]

Following the landmark publication in 1998 by Fire and Mellow, which eventually landed the pair a 2006 Nobel Prize in Physiology or Medicine, research in RNAi technology moved quickly. In 2001, Thomas Tuschl and colleagues at the Max Planck Institute for Biochemistry published a seminal paper in *Nature*, cited over 9,000 times and counting, which reported the use of synthetic 21-nucleotie RNA duplexes to target and suppress specific genes. This research ignited the commercial pursuit of RNAi drugs.

From 2002 to 2005, small, adventurous biotechnology firms such as Tekmira (then named Protiva) and Alnylam leaped into the development of RNAi therapeutics. Then, in a period from 2005 to 2008 defined by one commentator as an era of 'irrational exuberance,' big pharma invested $2.5-3.5 billion in the burgeoning field.[14] Peak-RNAi, so to speak, was reached when Merck and Roche paid $1.1 billion for acquiring Sirna Therapeutics and $300 million for a limited platform license from Alnylam, respectively. Dollars invariably attracted speculative investments in a yet unproven science.

In 2008, the walk of shame began. Although big pharmaceutical companies had aggressively pursued intellectual property related to RNAi technology, a viable therapeutic proved elusive. Setbacks, delays, negative clinical results and questions about the efficacy of basic RNAi therapeutics soon proved too much, and big pharmaceutical companies such as Roche, Pfizer, Merck and Abbott either divested or decommissioned in-house RNAi research capabilities.[15]

The RNAi space has yet to recover. From 2009-2012, pure-play RNAi therapeutics companies such as Tekmira generated a total of only $70-100 million in non-dilutive revenues (from licensing technologies

[9] *Nature Biotechnology* 32, 40-51 (2014). Clinical development success rates for investigational drugs. Michael Hay and David W Thomas et al. http://www.nature.com/nbt/journal/v32/n1/full/nbt.2786.html
[10] http://www.nobelprize.org/educational/medicine/dna/
[11] http://www.nature.com/nrg/multimedia/rnai/index.html
[12] http://www.nobelprize.org/educational/medicine/dna/
[13] *Pharmaceuticals* 2013, 6(1), 85-107. Nanoparticles-Based Delivery of RNAi Therapeutics: Progress and Challenges. Zhou and Shum et al.
[14] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3381602/
[15] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3381602/#bib6

and platforms or from government contracts). Compare this to the period from 2006-2009, when pure-play companies generated roughly $1 billion in non-dilutive revenues.[16]

To date, not a single RNAi therapeutic compound has successfully navigated the FDA approval process into clinical development.[17] Since the initial explosion of optimism, followed by a period of irrational exuberance, shoddy science and ill-advised investments, RNAi therapeutics have garnered a reputation as a wasteland of dollars and clinical disutility.

Recently, there has been a limited recovery in the field and cause for tempered optimism. Small NRAi molecules ("siRNA") released directly into the bloodstream were degraded by enzymes and unable to penetrate cell membranes. But some researchers, including Tekmira, have had limited success embedding siRNAs into lipid nanoparticles ("LNPs"). Testing in animal models indicated that in some instances such particles successfully ended up in the liver.[18] As a result, the bulk of promising RNAi drugs address diseases linked to the liver, including Tekmira's Hepatitis-B therapeutic technology.

The trouble is that Ebola infections do not specifically target cells in the liver. Rather, an Ebola infection also targets endothelial cells (cells lining the blood vessels), macrophages and monocytes (types of immune cells) throughout the body. The bio-distribution of Tekmira's LNPs is focused towards the liver, making it an added challenge to address diseases that target cells in other organs.[19]

It is not that TKM Ebola is certain to fail – it is just that it is highly, highly likely to fail. And right now, Tekmira's share price does not reflect the extremely low probability that TKM Ebola will be approved and adopted as a viable treatment.

[16] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3381602/#bib6
[17] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3381602/pdf/mtna20119a.pdf
[18] http://www.the-scientist.com/?articles.view/articleNo/40871/title/The-Second-Coming-of-RNAi/
[19] http://www.xconomy.com/national/2010/01/21/mercks-alan-sachs-on-rnais-big-challenge-delivery-delivery-delivery/?single_page=true

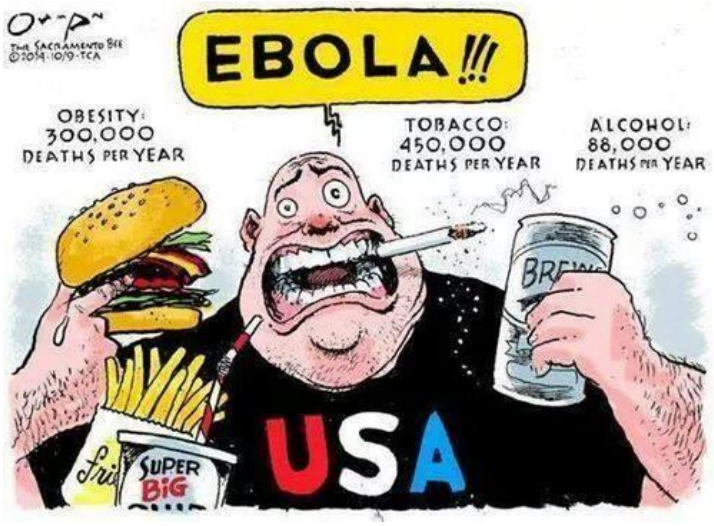
VALUATION: A BRIEF HISTORY OF STUPIDITY

Every so often, a small yet highly salient (and usually gruesome) threat emerges which, despite having a remote possibility of actually affecting a large number of people, captures our collective consciousness.

Following the attacks of September 11, 2001, someone[20] mailed deadly anthrax spores to NBC, the New York Post, and Sens Tom Daschle and Patrick Leahy. The attacks killed five people and induced a collective national hysteria. Although deadly, the panic was disproportionate to the threat. Anthrax is exceedingly difficult to weaponize, requiring advanced knowledge of biochemistry and sophisticated technology to grind the spores into small enough particles to infiltrate the lungs (where it can be deadly to humans). Despite the very small possibility that Anthrax could ever present a threat to the general public, absolute panic ensued.

One of the secondary (or even tertiary) effects of this delusional hysteria was that the stock price of companies with any connection to Anthrax soared. The share price of one such company, Palatin Technologies (NASDAQ: PTN), increased dramatically when on November 1, 2001, the biopharmaceutical firm announced a collaboration with the Walter Reed Army Medical Center to "evaluate the clinical utility" of the company's anthrax inhalation detector. Investors seemed to abandon rationality, forgetting that the anthrax threat was overblown and that the presence of such a threat did not make Palatin's unproven technology any more likely to succeed. Predictably, the price of PTN's stock collapsed when media hype regarding the Anthrax crises abated.

The recent Ebola scare is strikingly similar. In the United States, there have been nine confirmed diagnoses. One patient has died. The survival rate is 80% outside of Africa, and will only improve as hospitals and physicians in the United States increase their understanding of Ebola's pathology and become more practiced in available treatments.



Even though Ebola is not particularly easy to transmit from person to person, stupidity regarding Ebola has afflicted most of the population. A two-year college in Dallas recently denied admission to prospective students from Nigeria (a country who has to date reported roughly the same number of Ebola cases as the

[20] Interestingly, the FBI never conclusively identified the culprit.

Year to date, Tekmira's stock price is up over 100%, along with similarly massive gains in the price of shares of other Ebola companies such as CMRX (100%+ increase YTD) and BCRX (60%+ increase YTD).

We believe that Tekmira is hugely overvalued and that its share price is poised to collapse. RNAi technology is unproven, TKM Ebola's Phase I trial was halted over safety concerns, and nothing since, including limited application to two patients under exigent circumstances makes it any more likely that TKM Ebola is safe, efficacious and thus likely to gain FDA approval. In addition, there is evidence that treating physicians prefer other experimental treatments, and it appears that presumably due to concerns over TKM Ebola's safety risks, Tekmira's Ebola therapeutic is an experimental treatment of last resort. We therefore believe that Tekmira should be valued at its pre-Ebola valuation, between $7-10 per share.

DISCLAIMER

We are short sellers. We are biased. So are long investors. So is Tekmira. So are the banks that raised money for the Company. If you are invested (either long or short) in Tekmira, so are you. Just because we are biased does not mean that we are wrong. We, like everyone else, are entitled to our opinions and to the right to express such opinions in a public forum. We believe that the publication of our opinions about the public companies we research is in the public interest.

You are reading a short-biased opinion piece. Obviously, we will make money if the price of Tekmira stock declines. This report and all statements contained herein are the opinion of Glaucus Research Group California, LLC, and are not statements of fact. Our opinions are held in good faith, and we have based them upon publicly available facts and evidence collected and analyzed, which we set out in our research report to support our opinions. We conducted research and analysis based on public information in a manner that any person could have done if they had been interested in doing so. You can publicly access any piece of evidence cited in this report or that we relied on to write this report. Think critically about our report and do your own homework before making any investment decisions. We are prepared to support everything we say, if necessary, in a court of law.

As of the publication date of this report, Glaucus Research Group California, LLC (a California limited liability company) (possibly along with or through our members, partners, affiliates, employees, and/or consultants) along with our clients and/or investors has a direct or indirect short position in the stock (and/or options) of the company covered herein, and therefore stands to realize significant gains in the event that the price of Tekmira's stock declines. Use Glaucus Research Group California, LLC's research at your own risk. You should do your own research and due diligence before making any investment decision with respect to the securities covered herein. The opinions expressed in this report are not investment advice nor should they be construed as investment advice or any recommendation of any kind.

Following publication of this report, we intend to continue transacting in the securities covered therein, and we may be long, short, or neutral at any time hereafter regardless of our initial opinion. This is not an offer to sell or a solicitation of an offer to buy any security, nor shall any security be offered or sold to any person, in any jurisdiction in which such offer would be unlawful under the securities laws of such jurisdiction. To the best of our ability and belief, all information contained herein is accurate and reliable, and has been obtained from public sources we believe to be accurate and reliable, and who are not insiders or connected persons of the stock covered herein or who may otherwise owe any fiduciary duty or duty of confidentiality to the issuer. As is evident by the contents of our research and analysis, we expend considerable time and attention in an effort to ensure that our research analysis and written materials are complete and accurate. We strive for accuracy and completeness to support our opinions, and we have a good-faith belief in everything we write, however, all such information is presented "as is," without warranty of any kind– whether express or implied.

If you are in the United Kingdom, you confirm that you are subscribing and/or accessing Glaucus Research Group California, LLC research and materials on behalf of: (A) a high net worth entity (e.g., a company with net assets of GBP 5 million or a high value trust) falling within Article 49 of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "FPO"); or (B) an investment professional (e.g., a financial institution, government or local authority, or international organization) falling within Article 19 of the FPO.

Glaucus Research Group California, LLC makes no representation, express or implied, as to the accuracy, timeliness, or completeness of any such information or with regard to the results to be obtained from its use. All expressions of opinion are subject to change without notice, and Glaucus Research Group California, LLC does not undertake a duty to update or supplement this report or any of the information contained herein. By downloading and opening this report you knowingly and independently agree: (i) that any dispute arising from your use of this report or viewing the material herein shall be governed by the laws of the State of California, without regard to any conflict of law provisions; (ii) to submit to the personal and exclusive jurisdiction of the superior courts located within the State of California and waive your right to any other jurisdiction or applicable law, given that Glaucus Research Group California, LLC is a California limited liability company that operates in California; and (iii) that regardless of any statute or law to the contrary, any claim or cause of action arising out of or related to use of this website or the material herein must be filed within one (1) year after such claim or cause of action arose or be forever barred. The failure of Glaucus Research Group California, LLC to exercise or enforce any right or provision of this disclaimer shall not constitute a waiver of this right or provision. If any provision of this disclaimer is found by a court of competent jurisdiction to be invalid, the parties nevertheless agree that the court should endeavor to give effect to the parties' intentions as reflected in the provision and rule that the other provisions of this disclaimer remain in full force and effect, in particular as to this governing law and jurisdiction provision.