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UNITED STATES SENATE
SPECIAL COMMITTEE ON AGING

HEARING EXIBITS

"Sudden Price Spikes in Decades-Old Rx Drugs: Inside the Monopoly Business Model"

March 17, 2016 9:45 AM Dirksen Room 562

Susan M. Collins, Chairman
Claire McCaskill, Ranking Member

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Thanks for joining the Retrophin Thiola licensing call. Joining me is Marc Panoff, our CFO.

I'm on Slide 3. After the market close yesterday, we announced a license agreement with Mission Pharmacal, a family-owned, Texas-based drug company, for the U.S. rights to Thiola, or tiopronin. We are delighted to gain access to Thiola, an incredible medicine for people suffering from cystinuria. Thiola adds our marketed products portfolio, which we intend to expand further in the near future.

On slide 4, you can see this is a great deal for both companies. We are paying Mission a modest upfront payment, which will be disclosed in a future SEC filing. This upfront payment is small, and immaterial to Retrophin in the context of our balance sheet, which has recently expanded. We will pay Mission royalties on product sales.

Thiola is FDA approved for the treatment of cystinuria. The drug is taken to prevent kidney stone formation, the main sequelae of cystinuria. Thiola is considered the standard of care for this disease, and we will talk about that in more detail momentarily.

We believe Thiola has dramatic room for growth and peak sales of Thiola could reach 100 million dollars. We can promote Thiola with an active dedicated sales force, increase pricing, find new indications, increase diagnosis of cystinuria and begin thinking about selling Thiola in other geographies.

Finally, this drug fits hand-in-glove with Retrophin's portfolio. Every employee of Retrophin seems genuinely thrilled to gain access to this medicine.

Slide 5. Let's drill down on Thiola. IMS reports current Thiola revenue of approximately $2.1 million, which is the accurate current revenue for the product. Thiola is one of two molecules that are FDA-approved for the treatment of cystinuria. Penicillamine, which is available by two drug companies, is the other one. Penicillamine is generally seen to be much more toxic than Thiola. Amazingly, penicillamine is still 20 to 30 times more expensive than Thiola! The orphan drug status for Thiola has expired, and there are no approved generics. Interestingly, our tiopronin is the only approved tiopronin-based drug globally.

So, what is cystinuria? Slide 6. Cystinuria is one complex disease. Let's talk about the biology that underlies this disease. Two proteins come together, to form what we call a dimer. This heterodimer, composed of the SLC3A1 and SLC7A9 proteins, is responsible for re-absorbing cysteine and other amino acids from the kidney. When either of these proteins are mutated, cystinuria occurs. Cystine accumulates in the kidney and forms kidney stones. Cystine is insoluble at the pH levels of the kidney and urine and this precipitation causes chronic kidney stones that are excruciatingly painful. Not only are the cysteine stones extremely painful, but they are recurrent and frequent. Even worse, they are resistant to lithotripsy. The pain and suffering of cystinuria patients is something Retrophin is inheriting and seeks to change the face of. We take this responsibility extremely seriously and will be taking dramatic actions to change the lives of all cystinuria patients. I'll say more on this shortly.

Many cystinuria patients will never need Thiola. Cystinuria can often be managed by fluid intake and diet restriction. Unfortunately, some patients do need Thiola. Fluid intake is difficult to comply with and diet restriction is nearly impossible. Even with these approaches and alkalization therapy, some patients still develop kidney stones. There are only a few hundred patients on Thiola. Just like our product Chenodal, there are extremely few drug companies on the planet who will step up and care for

just a handful of patients. These small markets are attractive to Retrophin because we understand the plight of patients who are abandoned by the pharmaceutical industry.

Slide 7. An incredible number of people have cystinuria, and again, thankfully, many of them do not need Thiola. Still, cystinuria is one of the most common, but still rare, autosomal recessive diseases. Cystinuria is a global disease and as is typical, the United States, even though it has 20,000 cystinuria patients, has one of the lowest frequencies of cystinuria compared to other countries. Over time we will formulate a plan to bring Thiola to these global territories.

Slide 8. Cystinuria costs society an enormous amount. No number can be placed on the pain and suffering of having chronic kidney stones, but the procedures to remove kidney stones, combined with the ER visits, loss of productivity and pain take an enormous toll on our healthcare system. As I mentioned, the only other drug, which is seen as inferior to Thiola in terms of safety, is much more expensive than Thiola. We will normalize the price of Thiola to be competitive with penicillamine.

Retrophin plans a broad undertaking to enhance the value of Thiola to its patients. Thiola comes in an inconvenient 100mg pill format and this needs to be changed. Our great partner Mission, simply has other priorities and we have seen time and again that low-revenue drugs are extremely low priorities for almost all drug companies. Retrophin will certainly generate more revenue with a price increase on Thiola, but we will redeploy those profits in bringing people with cystinuria a better life. To us, this is the greatest win-win and we have won tremendous support from patients with similar actions we have taken on Chenodal.

Drug companies need to make a sufficient profit to continue supplying a drug. It is no accident that many small revenue drugs frequently have supply shortages. Thiola is no exception. Retrophin believes that every patient's life matters, no matter how rare the disease is. It is the truest tragedy if a patient has to endure pain and suffering because a drug company just isn't making enough revenue. Not only should product supply for rare diseases be steady, but there should be redundant supply for these crucial drugs. None of this is possible if a drug company is breaking even or LOSING money on a drug. Retrophin will make a comfortable, but not excessive <u>at all</u> profit, as our company has just broken even, while adding value to our most important constituent: our patients.

A steady and high-quality supply is not the only consideration in pricing a drug. Rare diseases like cystinuria are not focused on in the medical community, even by specialists. By sponsoring symposia and education, Retrophin can held remind physicians that this disease exists. We have heard from patients that this disease is often underdiagnosed or misdiagnosed. This is a terrible situation that falls on the drug company to manage. Again, a company breaking even or losing money on a drug is not incentivized to educate physicians on the rarest of diseases. With more revenue, we can afford our MSL and sales teams, who are very expensive I might add, and they can help eliminate some of the pain and suffering by shorting the time from diagnosis to treatment.

But that's not all. More revenue for Retrophin means we can fully support co-pays, ensuring no patient is left behind. We can investigate exporting our drug globally. We can fund research for an eventual cure for cystinuria. We can make new product forms that are more effective and convenient. All of these great additions to the healthcare ecosystem are possible when we take a higher price on a product. To this day we have never had a patient, patient group or physician complain about the price of a Retrophin product being too high. We asked cystinuria leaders if price increases for Thiola,

accompanied with the services mentioned, would be welcomed. The answer was a resounding and unanimous yes. We are proud of the steps we are undertaking to market Thiola and as our shareholders you should be proud to support us as well.

Slide 9. We are frequently asked about intellectual property and distribution strategy. Our distribution strategy for rare disease drugs is closed distribution. The closed distribution channel allows for higher patient service and care, including seamless co-pay reimbursement. These features are difficult to employ in the retail pharmacy setting. The closed distribution system also allows us to control the release of our product. We do not sell Retrophin products to generic companies. The only people who need Thiola and should be able to buy it are patients who are suffering from cystinuria.

The specialty pharmacy distribution model takes the AB substitutable rating that generics get and neuters it. Because of the extremely high-touch service we provide, and the sole distributor we have, the AB rating for a putative, and in my opinion, unlikely to occur, generic is ineffective. AB substitutability is useful when a pharmacy can automatically substitute a prescription for a generic at the pharmacy level. This whole model that generics rely upon is turned upside down with specialty pharmacy distribution.

Most importantly, we intend to discontinue Thiola 100mg tablets over time. Thiola should be made available in 250mg and 500mg tablets. With our partner Mission, we hope to provide a more convenient solution for patients who usually need 800mg of drug per day. Finally, an extended release version of Thiola would further enhance compliance and treatment. Our intent is to remove our legacy products from the channel as soon as new products are available, which is often called a "hard switch". Given all of these dynamics and the likely low revenue of Thiola even after a price increase, we do not believe generics will enter the market for this product anytime soon, if ever. Chenodal and Vecamyl are similar Retrophin products with these dynamics.

On Slide 10 you can see that we are raising guidance for 2014 and 2015. We had previously given guidance of $20 to $22 million in revenue for 2014. We are raising that guidance to $30 to $35 million, to reflect the seven months we will own Thiola and continued confidence in Chenodal and Vecamyl. Our 2015 guidance is being raised from $36 to $41 million to $60 to $70 million. I believe this guidance is conservative and I look forward to updating it as time goes on.

Over time, Thiola could become a $100 million product. This is an aspiration goal and not at all reflected in our guidance. Given the cost of the product license, which is de minimus, and the forecasted revenue and likely lifecycle of the product, we believe the license of Thiola has added approximately ten dollars per share in value to our company. I'd like to thank our hard-working business development team, including Courtney Bond, the executive who discovered the Thiola opportunity, for their contribution to the company. I truly believe we have the best BD team in the pharmaceutical industry.

I have been valuing pharmaceutical companies the same way for over 10 years. I believe drug companies should capitalize research and development costs. Unfortunately, accounting standards require that they are expensed. Increasingly, we have seen pharmaceutical companies spend less on R&D because of this dynamic. Acquisition of R&D allows drug companies to use their balance sheet, instead of their income statement, to conduct R&D. It is easy for a financial analyst to strip out R&D and other one-time-like costs to assess what the true earnings power of a company is. R&D is a one-time cost for Retrophin. As the largest shareholder of the company, I promise you, that if our R&D efforts do not bear fruit, we

will slash R&D to zero. Also, R&D is unrelated to revenue. Thiola, Chenodal and Vecamyl will generate the amount of revenue they are destined to generate whether we spend zero on R&D or $100 million on R&D. The idea that R&D is a part of the income statement of our company makes sense from an operating perspective because cash leaves the company, but it really belongs on the cash flow statement and balance sheet, because I view R&D as an investment.

As a result of these dynamics, we disclosed last quarter our metric called earnings power per share. This is the EPS number we could generate if we adjusted our business model to exclude R&D and made other adjustments. The number is really supposed to represent the buy-able earnings power if we were acquired by the average pharmaceutical company. In our last quarterly call, I mentioned that I believed our earnings power was one dollar per share. Today, after the Thiola deal, I believe our earnings power per share is 1.50 to 2.00 per share, and that is likely to be conservative.

Our business development pipeline is extremely robust. We plan on announcing another deal in the next 90 days, and possibly a lot sooner. We recently had the opportunity to bid 250 million dollars on a portfolio of pharmaceutical assets. We were able to privately and confidentially raise money for this potential transaction quickly and easily. While the transaction did not close for irrelevant reasons, I am delighted that we were able to access so much capital so quickly. Retrophin is looking at opportunities up to one half of a billion dollars for acquisitions, as well as smaller deals like Thiola. Stay tuned as we continue to try to grow our earnings. My sole focus is a growing EPS over time, including an R&D spend that will enhance our long-term growth. Our stock price is not a focus for me. There is no realistic benefit that comes from a high stock price and those of you who know us well understand that this is a deeply held opinion at Retrophin. With no analyst coverage, no conference presentations, no IR people, and very infrequent roadshows, we are focused on growing our business, not growing our stock price.

Our capital raise of $80 million is very gratifying. As I mentioned, Retrophin had no need to dilute unless it found an attractive deal. I believe the Thiola transaction adds hundreds of millions of dollars to the value of our company with extremely small risk. Our new partner, Athyrium, was awarded the senior debt opportunity that we seeked. This competitive process was extremely well managed by Barclays, one of the best healthcare investment banking groups, and we are delighted to work with Athyrium. The ability for a company like Retrophin to tap the debt markets is truly flattering. Most biotech companies never get a chance to issue debt. Over time we expect our debt coupons to drop as we establish a track record of cash flow. We'd also like to thank our convertible note investors. Convertible debt is equity-like, but the small amount of dilution this debt represents allows us to pursue further Thiola-like deals and strengthens our relationship with our equity shareholders, who were the main buyers of our convertible debt.

A quick word on PKAN. We are encouraged by our early experience with our first European patient. We will be releasing 28-day data on this patient next month. The only thing we are reporting at this time is that we are encouraged by the data thus far and the drug is extremely well tolerated. More patients are in the pipeline to be enrolled in investigator-led emergency trials for RE-024. I look forward to updating you on that, potential further acquisitions and our revenue and earnings progress soon.

With that, I'll take any questions you might have.

From: Edwin Urrutia
To: Dan Wichman [redacted]
CC: Martin Shkreli
Sent: 5/20/2015 3:49:27 PM
Subject: Turing Transaction
Attachments: Turing Mutual CDA.docx

Dan,

Hope all is well. We are working on a few transactions at Turing that we want to discuss with you. If it makes sense let's discuss over a call or meeting. I have attached our standard CDA so we can get into the details.

Transaction 1:

Potential licensing deal for a $6mm revenue product. Product is sole sourced and the standard of care for a life threatening indication. Current pricing is low relative to the value it provides. We plan to place product in a closed distribution system (e.g. Thiola and Chenodal). Currently there is no salesforce and we plan to hire a dedicated salesforce and focus on disease awareness. Ability to extend life cycle by developing modified formulations and working on analogues.

This is a $2B+ NPV opportunity for us. We believe we can get this to $200mm in revenue per year. We have made an initial offer for an upfront payment between $15mm - 20mm, 15% royalties on net sales to seller and a recurring annual license fee. Our plan is to finance this through equity.

Transaction 2:

Potential acquisition of $10mm revenue product. The product is also sole sourced and the standard of care for the indication. This product is not priced appropriately to the value it provides. We plan to place product in closed distribution, hire a dedicated salesforce and focus on disease awareness. We can extend cycle through combo formulation, once daily formulation and next generation analogues.

This is a $2B+ NPV opportunity for us as well. We believe we can get this to $300mm in revenue per year. We have made an initial offer of 6x sales for a total purchase price of $60mm. We plan to finance this with a mixture of debt and equity.

We are in advanced discussions with both parties and the transactions could move quickly.

Best,
Edwin

Edwin Urrutia
Turing Pharmaceuticals AG
[redacted]

Retrophin

Manchester Pharmaceuticals Acquisition
February 13, 2014

Retrophin

Forward-Looking Statements

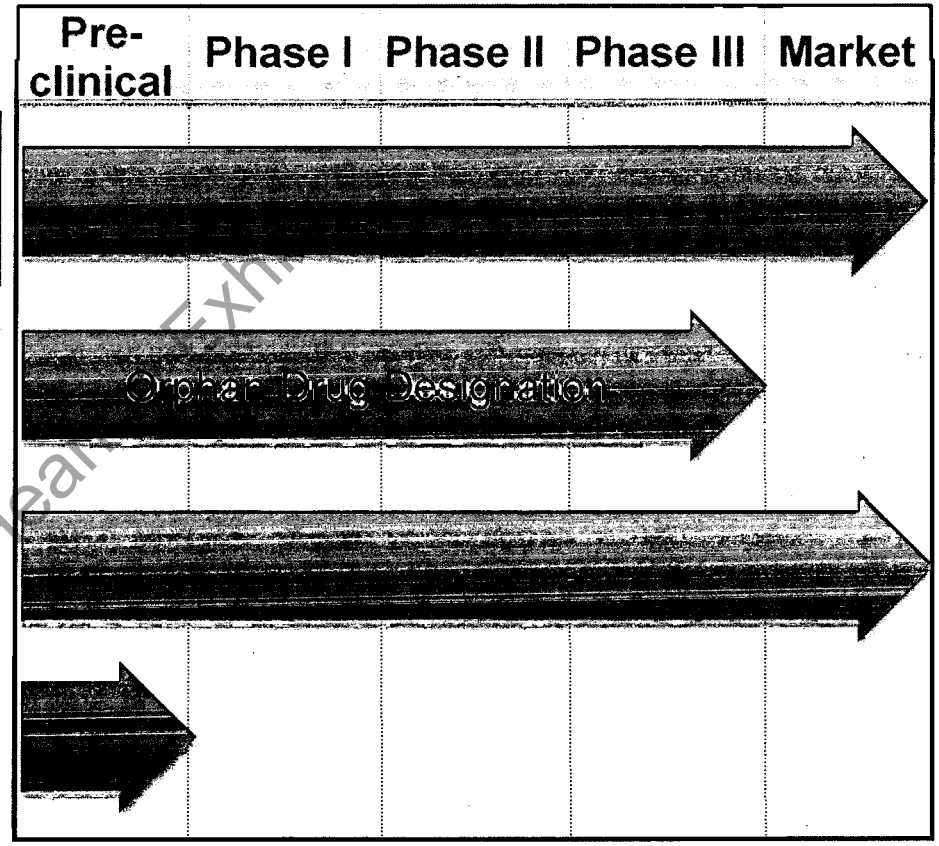
This presentation contains forward-looking statements, including statements about our prospects, competitive position, regulatory filings and agency actions, and the anticipated development, timing, data readouts and therapeutic scope of programs in our clinical pipeline. These forward-looking statements may be accompanied by such words as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "project," "target," "will" and other words and terms of similar meaning. You should not place undue reliance on these statements.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including the safety and efficacy of our product candidates, product competition, the occurrence of adverse safety events with our products, adverse market and economic conditions, our dependence on collaborations and other third parties over which we may not always have full control, failure to comply with government regulation, our ability to protect our intellectual property rights, and have sufficient rights to market our products and services together with the cost of doing so, problems with our manufacturing processes and our reliance on third parties, our ability to attract and retain qualified personnel, our level of indebtedness, environmental risks, change of control provisions in our collaborations and the other risks and uncertainties that are described in the Risk Factors section of our most recent annual or quarterly report and in other reports we have filed with the SEC.

These statements are based on our current beliefs and expectations and speak only as of the date of this presentation. We do not undertake any obligation to publicly update any forward-looking statements.

Acquisition – Manchester Pharmaceuticals

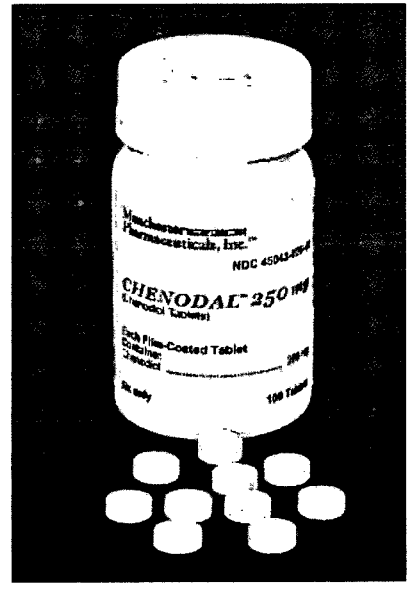
Chenodal	Gallstones
Chenodal	Cerebrotendinous xanthomatosis
Vecamyl	Hypertension
Vecamyl	Rage Disorders



Overview

- Retrophin to acquire Manchester Pharmaceuticals
  - Privately-held specialty pharmaceutical company with two FDA-approved products
    - Chenodal® (chenodeoxycholic acid)
    - Vecamyl® (mecamylamine)
- $62.5m purchase price
  - $29.5m paid upfront
  - Remaining payments to be delivered over 2014
  - Ongoing royalty on sales
- Highly accretive acquisition creates a fully-integrated specialty pharmaceutical company focused on catastrophic diseases

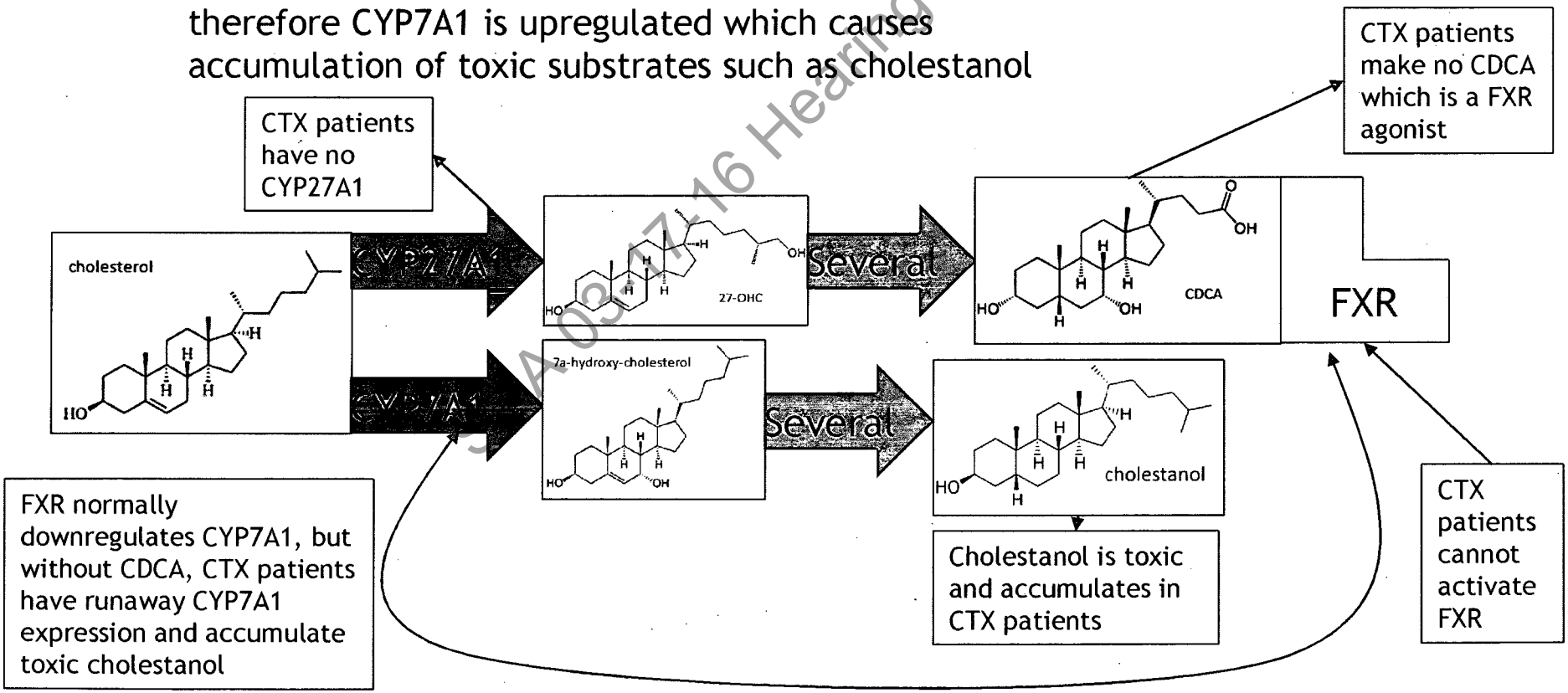
Chenodal® (chenodeoxycholic acid)



- Chenodal (CDCA) is a synthetic bile acid approved for the treatment of gallstones, but...
- ...usage is exclusively in **cerebrotendinous xanthomatosis (CTX)**
  - CDCA is the standard of care for CTX
  - Chenodal is the only FDA-approved formulation of CDCA in the U.S.
    - Manchester received FDA approval of Chenodal in 2009
- Chenodal received Orphan Status for CTX in 2010
- Retrophin will file for approval in CTX in 2014
- Pricing for Chenodal is ~$110,000 per patient per year
  - Retrophin believes there is upside to this price and will increase price to accommodate product expansion and patient identification efforts

Cerebrotendinous Xanthomatosis (CTX)

- Inborn error (autosomal recessive) of metabolism
  - Mutation in CYP27A (sterol-27-hydroxylase)
    - This enzyme converts cholesterol to CDCA
    - CDCA binds to FXR and downregulates CYP7A1, which generates bile acids from cholesterol
    - Patients with CTX mutations cannot make CDCA and therefore CYP7A1 is upregulated which causes accumulation of toxic substrates such as cholestanol



Cerebrotendinous Xanthomatosis (CTX)

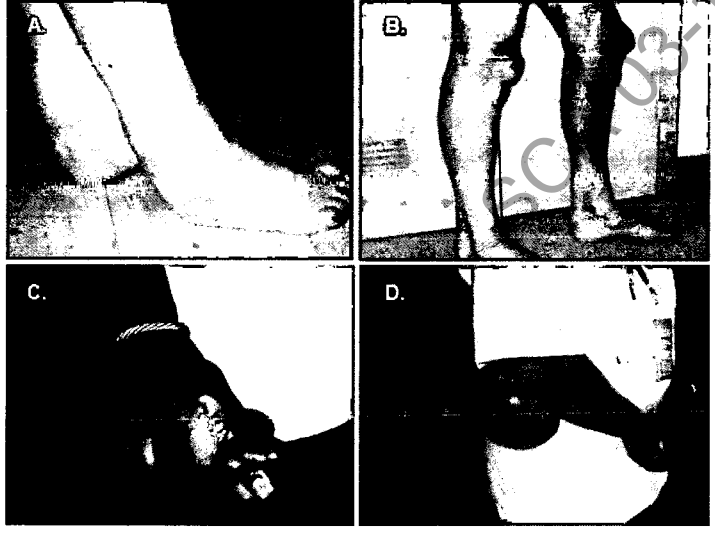
- CTX is a very difficult diagnosis to make
  - CTX patients begin life with neonatal cholestatic jaundice and refractory diarrhea
    - These common, non-critical and non-specific symptoms rarely lead to a CTX diagnosis
  - Disease progression then occurs with juvenile cataracts, tendon xanthomas (lipid deposition) and neurological deterioration (motor dysfunction, intellectual disabilities)
    - 95-97% of CTX patients have neurological symptoms at diagnosis
  - The disease can be lethal without Chenodal treatment

CTX Epidemiology

- Due to the underdiagnosis of CTX, epidemiology data are limited
  - Published speculation of 1/1,000,000 to 1/50,000 prevalence
- Retrophin believes there are at least 500 - 1,000 U.S. CTX patients
  - Currently <5% - 10% are diagnosed / treated
- Retrophin believes that many CTX patients are **misdiagnosed** due to a lack of awareness and variable and non-specific presentation
  - An in-house survey of 5 KOLs who treat CTX patients estimate the incidence to be much higher than patients who are currently dosed
- Retrophin is confident that doctor awareness, newborn genetic screening and establishing a patient registry will rapidly identify more patients in the US and ROW

Chenodal in CTX

- Chenodal replacement therapy is functionally curative for CTX patients
  - Measured by serum cholestanol
  - Healthy patients have little-to-no serum cholestanol
  - After Chenodal treatment, cholestanol drops ~98%
- Chenodal was never subjected to a clinical trial for CTX given its off-label discovery of efficacy
  - We believe a clinical trial would be unethical
  - Standard-of-care-status is unquestioned



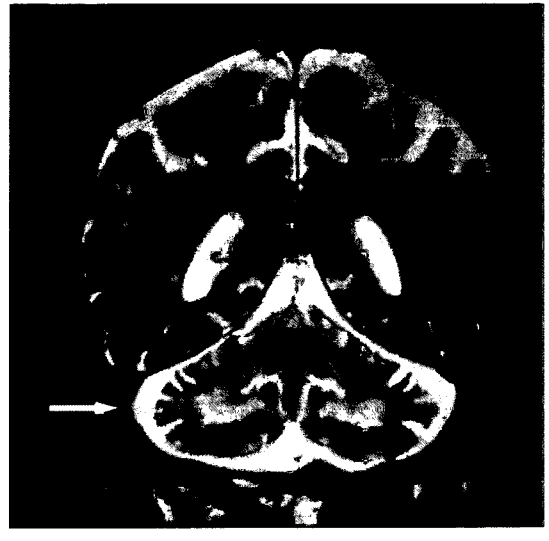


Fig 2. Cerebellar atrophy and hyperintense sign in dentate nuclei and adjacent cerebellar white matter on T2-weight RMI images (arrow), for a patient with cerebrotendinous xanthomatosis.

Chenodal Pricing

- Price per patient per year (PPPY)
  - Wall Street focuses on this
- % of healthcare spend
  - Insurers focus on this

	US Revenue	Cost to HMO	Annual Cost / Life Covered	% of HMOs drug spend	PPPY	Generic Alternative?
Humira	6,668	1,000	24.40	1.334%		YES
Abilify	6,076	911	22.23	1.215%		YES
Januvia	3,120	468	11.41	0.624%		YES
Soliris	560	84	2.05	0.112%	450,000	NO
Fabrazyme	267	40	0.98	0.053%	300,000	NO
Cerezyme	239	36	0.87	0.048%	300,000	NO
Kalydeco	200	30	0.73	0.040%	307,236	NO
Myozyme	168	25	0.61	0.034%	600,000	NO
Elaprase	150	23	0.55	0.030%	500,000	NO
Vpriv	100	15	0.37	0.020%	300,000	NO
Naglazyme	50	8	0.18	0.010%	750,000	NO
Chenodal	5	1	0.02	0.001%	113,520	NO
Total Ultra-Premium Price Segment				**0.348%**		

Global Opportunity

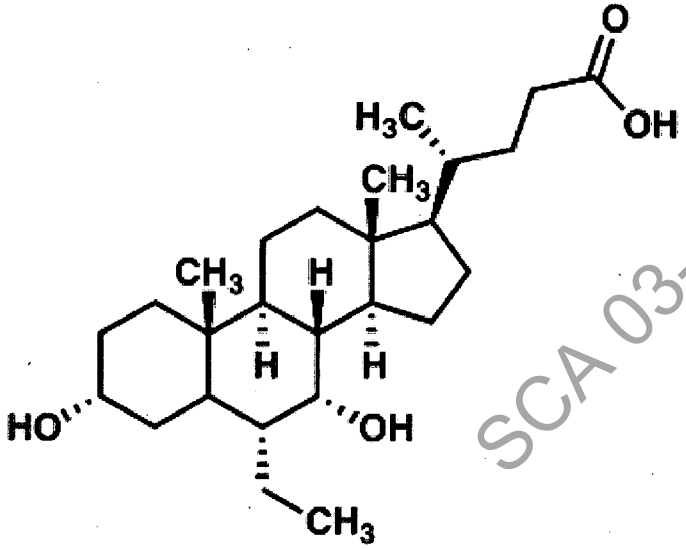
- Current supply of the only other available chenodeoxycholic acid product is limited to ROW markets and is spotty
  - Several product availability complaints
- Retrophin believes a large international opportunity exists
  - At least 1,000 international patients undiagnosed, untreated and without an alternative product
- ROW revenue is usually 50-90% of total revenue for most orphan drugs
  - Zero ROW revenue today
  - Retrophin targets at least 50% ROW revenue long-term

Intellectual Property

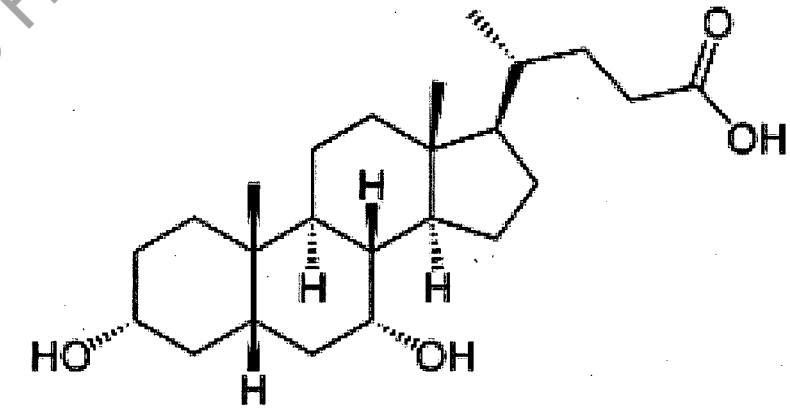
- Retrophin will seek FDA approval for Chenodal in CTX this year
  - Expect rapid approval and 7-year orphan status
- Centric specialty pharmacy distributor
  - Closed distribution system does not allow for generics to access product for bioequivalence study
    - ANDA filings are impossible unless generic company illegally penetrates specialty distributor
    - Recent *Celgene v. Lannett* case establishes precedent
- Retrophin plans to develop a once-a-day chenodeoxycholic acid and remove Chenodal from distribution at the appropriate time

Other Indications

- FXR agonism has become a popular MOA and reaches across several therapeutic areas including hepatology and nephrology
- Possible additional indications for Chenodal include primary biliary cirrhosis (PBC) and nonalcoholic steatohepatitis (NASH)



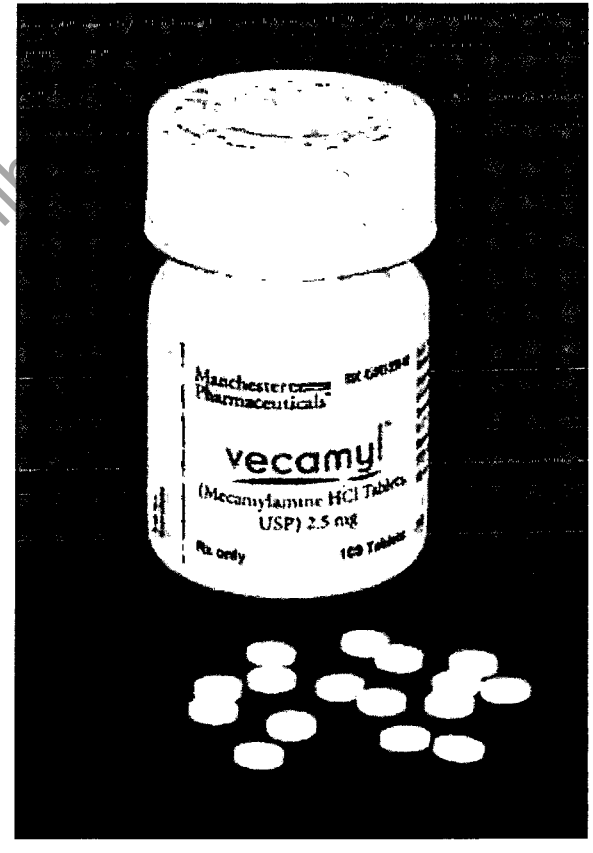
Obeticholic acid (OCA)



Chenodeoxycholic acid (CDCA)

Vecamyl®

- Vecamyl has exhibited strong growth since its reintroduction to the market with no marketing
  - Retrophin is aware of off-label use in rage associated with autism spectrum disorder
- Retrophin plans to continue to make Vecamyl available but does not intend to engage in any marketing or promotional activities



Forecasts

- 2014 revenue guidance of $10 - $12 million
- 2015 revenue guidance of $19 - $21 million
- Manchester EBITDA margins of 75-80%
- Potential peak sales of $100-$250 million

We estimate NPV of acquisition of Manchester of at least ~$10 per Retrophin share

Thank You!

Retrophin

TURING
PHARMACEUTICALS

Project Dart

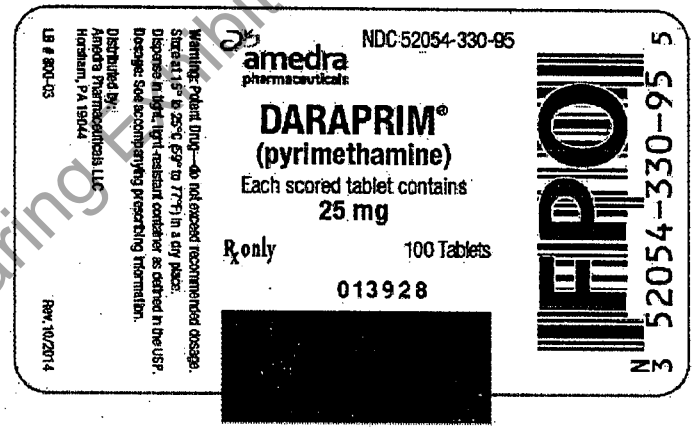
June 2015

Executive Summary

- **Turing is in discussions to acquire Daraprim® (pyrimethamine) from Impax Labs (IPXL)**
  - 2014 US net revenue of $4.9mm
  - Initial offer of 6x 2014 US net sales ($29.5mm)
- **Daraprim® is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide, since synergism exists with this combination**
  - FDA approved in January 1953 (NDA #008578)
  - Gold standard of care for toxoplasmosis
- **Turing is looking to borrow $5mm – $15mm in senior secured debt**
  - The transaction will be financed with a combination of debt and equity
- **We believe there are several potential strategies to grow revenue**
  - Current pricing lower than other adjunctive therapies
  - Daraprim® fits the specialty distribution business model

Daraprim Prescribing Information and Pricing

- **Daraprim® is indicated for the treatment of toxoplasmosis encephalitis**
  - Approved January 23, 1953
  - No approved generics or recent DMFs
- **Current gold standard for Toxoplasmosis**
  - Co-administered with sulfadiazine
  - Inhibits DHFR, disrupting folate synthesis
- **Dose: 50 – 75mg/day**
  - 25mg, 100 count bottle
  - ~$3,000 PPPY
- **Payor Mix**
  - 45% Commercial
  - 25% Medicaid
  - 25% Medicare Part D
  - 5% Cash



Actual	2011	2012	2013	2014	Q1:2015
Units (bottles)	12,600	11,004	10,260	9,708	1,836
Net Sales (mm)	$5.114	$5.620	$5.829	$4.932	$1.226

Gross-to-Net Calculation

- Chargebacks may be specific to Impax's current contracts with group purchasing organizations (GPOs) and managed care
  - Current pyrimethamine chargeback terms likely a result of negotiated terms for a larger Impax portfolio

	2011	2012	2013	2014	Q1:15
Gross Revenue	9,138,946	10,650,678	12,067,428	13,146,270	2,488,661
Cash Discount	182,779	213,014	241,348	256,317	51,003
Medicaid	1,104,817	1,812,187	2,878,267	3,348,557	699,472
Returns	673,025	532,534	241,176	1,061,405	(72,997)
Rebates	612,949	746,747	683,141	864,634	183,242
Discount Rebate	-	-	10,056	9,765	2,290
Chargebacks	1,450,864	1,725,553	2,183,854	2,673,073	398,986
Net Revenue	**5,114,512**	**5,620,644**	**5,829,586**	**4,932,521**	**1,226,665**
Units	12,576	11,004	10,260	9,708	1,836
Px/unit	727	968	1,176	1,354	1,355
Realized Px/unit	407	511	568	508	668
Cash Disc	2.0%	2.0%	2.0%	1.9%	2.0%
Medicaid	12.1%	17.0%	23.9%	25.5%	28.1%
Returns	7.4%	5.0%	2.0%	8.1%	-2.9%
Rebates	6.7%	7.0%	5.7%	6.6%	7.4%
Dis Rebate	0.0%	0.0%	0.1%	0.1%	0.1%
Chargebacks	15.9%	16.2%	18.1%	20.3%	16.0%
Net Revenue	56.0%	52.8%	48.3%	37.5%	49.3%

Toxoplasmosis Overview

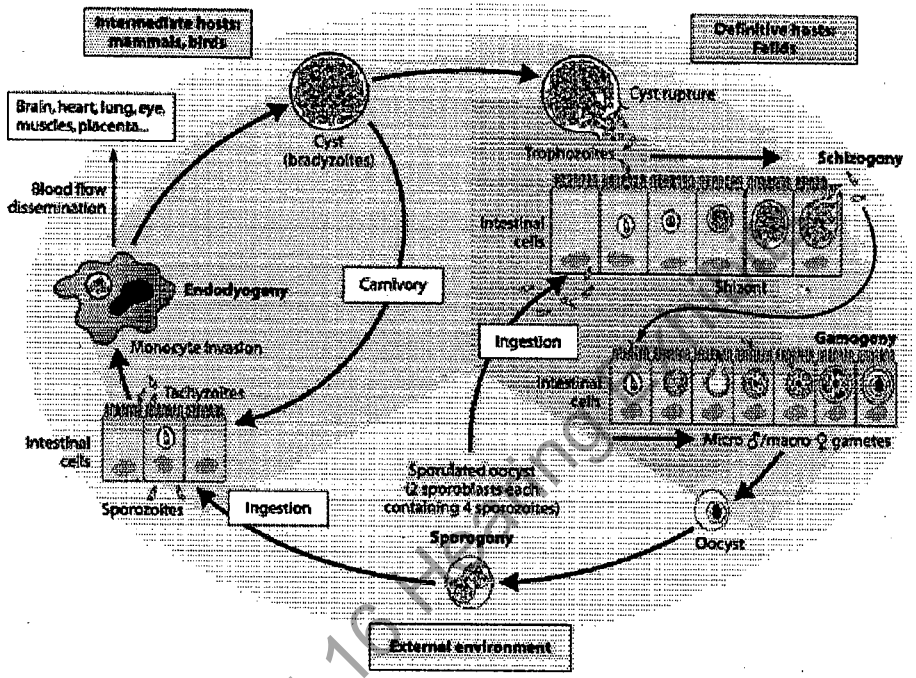


FIG 2 Life cycle of *Toxoplasma gondii*. Shown are the biology, infection, and replication of the three infective stages of the parasites in their respective hosts.

- Approximately 15% of US population is seropositive for toxoplasmosis (30% worldwide, >50% in Brazil)
- Patients become infected by ingesting cysts in undercooked pork or oocysts in contaminated water
- Toxoplasmosis can cause severe neurological, ocular, and systemic diseases in neonates and individuals with weakened immune systems
- Symptoms self-resolve in immunocompetent hosts, though cysts containing dormant bradyzoites will remain throughout life, predominantly in the brain, CNS and musculature

<u>Toxoplasmosis is always life threatening for neonates and the immunocompromised</u>

Toxoplasmosis Clinical Presentation

Immunocompromised Patients

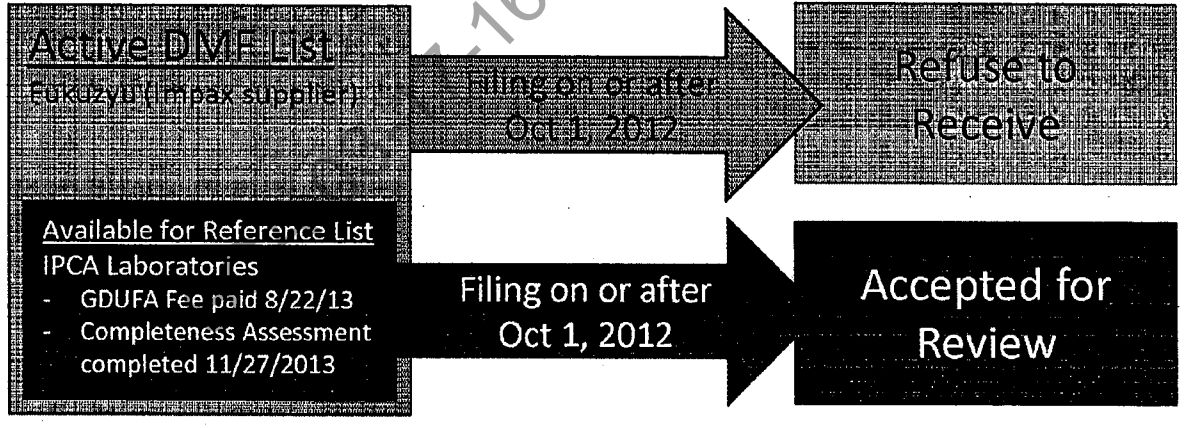
- Majority of patients are HIV positive with CD4+ counts < 100
  - Occasional incidence in immunosuppressed transplant patients
- Initially presents with non-specific symptoms such as headache, lethargy, and fever
- Disease is usually identified when patients present with difficulty walking, weakness on one side of the body (hemiparesis), seizure, speech abnormalities and loss of memory
- If untreated, further cerebral necrosis leads to dementia, status epilepticus, coma and death
- Primary lesions of cerebral necrosis, but retinal lesions are common if the infection disseminates to the eye, which can lead to blindness

Congenital Toxoplasmosis

- Estimated incidence of 1:10,000 births
- Risk of infection increases with each trimester, but infections in the first trimester lead to the most severe disease
- Congenital infection can lead to a wide variety of manifestations including spontaneous abortion, hydrocephalus or microcephalus, CNS calcification, retinochorioditis, and failure to thrive
- Symptoms that present later in infancy and childhood include learning disabilities, growth retardation, mental retardation, convulsions, palsies, blindness and deafness

New Entrant Feasibility

- Under GDUFA, ANDAs filed on or after October 1, 2012 referencing Type II DMFs must use a DMF listed on the "Available for Reference" list to avoid receiving a "Refuse to Receive" response from FDA
- Turing believes an ANDA was likely filed in 2014 using IPCA's API
  - FDA released bioequivalence guidance for pyrimethamine in March 2015, likely in response to an earlier filing
  - Fukuzyu currently in an exclusive supply agreement with Impax and not listed as "Available for Reference"



New Entrant Feasibility

- **Data Integrity is a very important issue for FDA**
  - IPCA will have to conduct very rigorous review of data reporting standards
  - Any ANDAs currently on file will likely be put on hold
- **Potential filer may stay with IPCA**
  - IPCA has confirmed that they will be unable to supply pyrimethamine for at least 12 months
    - Independent consultants believe this timeline is "very aggressive"
  - Citizens petition could further delay any ANDAs filed with IPCA supply
  - There is no protocol for lifting import bans, which may delay process further
- **Potential filer may have moved to a new vendor**
  - Appearance in the "Available for Reference" list will signal the refiling/amendment
  - Filer will need to requalify any API and re-validate processes and methods
  - Additional 6 months minimum for long term and accelerated stability
  - Major amendment to ANDA will further delay review date
  - FDA may allow filing without additional bioequivalence
- **Turing believes Daraprim will remain sole source until at least mid 2016**
- **If no developments have occurred by 2016, Turing believes Daraprim could remain a single source product much longer**

Lifecycle Management

- **Line extensions**
  - Once-a-day pill
  - Combination with sulfadiazine
- **Next generation analogues**
  - No new medicines have been approved in more than 40 years
  - Improved potency, avoid teratogenicity
  - Target T. gondii DHFR
    - Pyrimethamine more active against human DHFR
- **Toxoplasmosis Vaccine**
  - Academics have made progress in several vaccines targeting various surface antigens
    - SAG1

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Experienced and Fast-Growing Commercial Team

Executive	Experience
Nancy Retzlaff *Chief Commercial Officer*	• More than 20 years of biopharmaceutical commercial leadership experience including sales, marketing, commercial development & business leadership roles at Bayer, Schering-Plough, Pfizer & Mesoblast
Richard DeYoung *Head of Sales & National Accounts*	• More than 15 years of biopharmaceutical experience leading sales, key accounts and managed markets teams at Takeda and Astra Zeneca
Tina Ghorban *Senior Director, Business Analytics & Customer Insights*	• 15 years of biopharmaceutical experience in market analytics, global commercial development, new product marketing and US marketing at Pfizer, Shionogi and Mesoblast
Scott Emmens *Sales Director*	• 15 year biopharmaceutical sales leadership experience including sales operations and sales training at Astra Zeneca, Takeda and Shire

Relevant Experience and Skill Sets:

- Therapeutic areas of expertise include orphan & rare diseases and broader disease areas (HIV, pain, IBD, anemia, diabetes, cardiovascular, respiratory, endocrinology, CNS)
- Experience across broad range of product lifecycles, including global and US launches, mature brands, peri-LOE and branded generics
- Creation of complete commercial organization and infrastructure, as well as leading organizations through dynamic change and growth
- Alignment of marketing & sales around a specialty distribution strategy and patient services platform
- Creation of strategic brand platform, market development plan, and communication platforms. Tactical execution of all planned activities.
- Strategic planning and execution with all key customers, including KOLs, physicians, payers, patients and patient advocacy

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Financial Projections

- **Toxoplasmosis is a rare disease and should be priced appropriately**
  - Current Hepatitis C cost for cure > $100,000
  - Net present value of HIV treatment > $250,000
  - Both significantly more prevalent and have multiple treatment options
- **Turing management has experience with similar revenue growth strategies while at Retrophin**
  - Specialty sales force
  - High-touch closed distribution system
  - Improved patient advocacy and support
- **Potential revenues of over $500mm with greater than 80% EBITDA margins**
- **Turing plans to finance the transaction with a combination of debt and equity**

Financial Model

- Illustrative Model
  - Assumes $200,000 per unit

	2011	2012	2013	2014	Partial 2015	Full 2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Net Revenue (mm)	**5.1**	**5.6**	**5.8**	**4.9**	**336.5**	**339.2**	**854.7**	**880.4**	**90.7**	**9.3**	**1.0**	**1.0**	**1.0**	**1.1**	**1.1**	**1.1**
Total COGS	0.6	0.5	3.6	0.4	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Gross Profit	4.5	5.1	2.2	4.5	333.5	336.2	851.7	877.4	87.7	6.3	-2.0	-2.0	-2.0	-1.9	-1.9	-1.9
R&D	0.0	0.0	0.0	0.0	4.0	4.0	4.0	4.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sales Force	0	0	0	0	50	50	200	200	0	0	0	0	0	0	0	0
FTE Salary	0.0	0.0	0.0	0.0	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.255	0.260	0.265	0.270
Sales & Marketing	0.0	0.0	0.0	0.0	3.8	3.8	7.6	7.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
G&A	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OPEX	1.0	1.0	1.0	1.0	8.8	8.8	12.6	12.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Operating Income	**3.5**	**4.1**	**1.2**	**3.5**	**324.8**	**327.4**	**839.1**	**864.7**	**87.7**	**6.3**	**-2.0**	**-2.0**	**-2.0**	**-1.9**	**-1.9**	**-1.9**
Interest Expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest Income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	21.3	37.9	40.3	41.2	41.9	42.7	43.4	44.2	45.0
Pre-tax Income	3.5	4.1	1.2	3.5	324.8	327.4	839.1	886.0	125.6	46.6	39.1	39.9	40.7	41.5	42.3	43.1
Taxes	0.2	0.2	0.1	0.2	19.5	19.6	50.3	53.2	7.5	2.8	2.3	2.4	2.4	2.5	2.5	2.6
Net Income	**3.3**	**3.9**	**1.2**	**3.3**	**305.3**	**307.8**	**788.8**	**832.8**	**118.1**	**43.8**	**36.8**	**37.5**	**38.3**	**39.0**	**39.8**	**40.5**
EPS	1.66	1.94	0.58	1.65	152.64	153.90	394.40	416.42	59.04	21.92	18.40	18.76	19.13	19.50	19.88	20.27
S/O	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Cash Balance				-30	276	276	1,064	1,897	2,015	2,059	2,096	2,134	2,172	2,211	2,251	2,291
Debt				0	0	0	0	0	0	0	0	0	0	0	0	0
Net Cash	0	0	0	-30	276	276	1,064	1,897	2,015	2,059	2,096	2,134	2,172	2,211	2,251	2,291
Gross Margin				91%	99%	99%	100%	100%	97%	68%	-212%	-203%	-194%	-185%	-177%	-169%
OPEX				20%	3%	3%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
R&D				0%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
S&M				0%	1%	1%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
G&A				20%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Operating Income				71%	97%	97%	98%	98%	97%	68%	-212%	-203%	-194%	-185%	-177%	-169%
Net Income				67%	91%	91%	92%	95%	130%	469%	3825%	3786%	3748%	3710%	3672%	3635%

0 Debt
0% Coupon

0 Equity
0 Share Px
0.0 New Shares
2.0 S/O

0 Total Raise
30 Purchase Px
8.0x Multiple

7.0% Discount
2,028 NPV

TURING
PHARMACEUTICALS

Project Dart

June 2015

December 22, 2015

Ron Tilles
Interim CEO
Turing Pharmaceuticals
1177 Avenue of the Americas, 39th Floor
New York, NY 10036

Dear Mr. Tilles:

We write with the hope that in your new role as Interim CEO of Turing Pharmaceuticals you will lead the company in a new direction that places patient interests and lives ahead of short-term profits.

As a first step, we urge you to immediately return the price of pyrimethamine (marketed as Daraprim®) to $13.50 – the price it had been prior to Turing's acquisition of rights to produce this medication. Despite Turing's repeated assurances to the contrary, the $750 per tablet price has wreaked serious havoc on patient access to treatment of toxoplasmosis resulting in treatment delays and interruptions. In addition to the negative impact on patients, the controlled distribution system and the need for many patients to access the medication through the Daraprim Direct patient assistance program have placed significant and costly strains on medical providers and the health care system. Based on the drug's price of $1 per tablet or less outside of the U.S., the $13.50 price per tablet would allow for a profit of at least $12 per tablet—a profit margin that should be more than adequate to sustain providing this lifesaving medicine to patients.

We are deeply concerned about the long-term impact of Turing's business strategy that relies on setting extraordinary prices for decades old lifesaving medications, such as pyrimethamine, to sustain Turing's investment and research portfolio. The assumption that these costs can be borne by hospitals and public and private health care payers, and that complex mitigation strategies will prevent patient harm, is very risky with the risk primarily being borne by patients.

We appeal to you as Turing's Interim CEO to chart a new course for the company by making pyrimethamine readily accessible and affordable, at the $13.50 per tablet price, so that providers and patients have access to the medication when and where they need it. Patients' lives and our nation's public health are depending on your leadership. We look forward to your reply.

Sincerely,

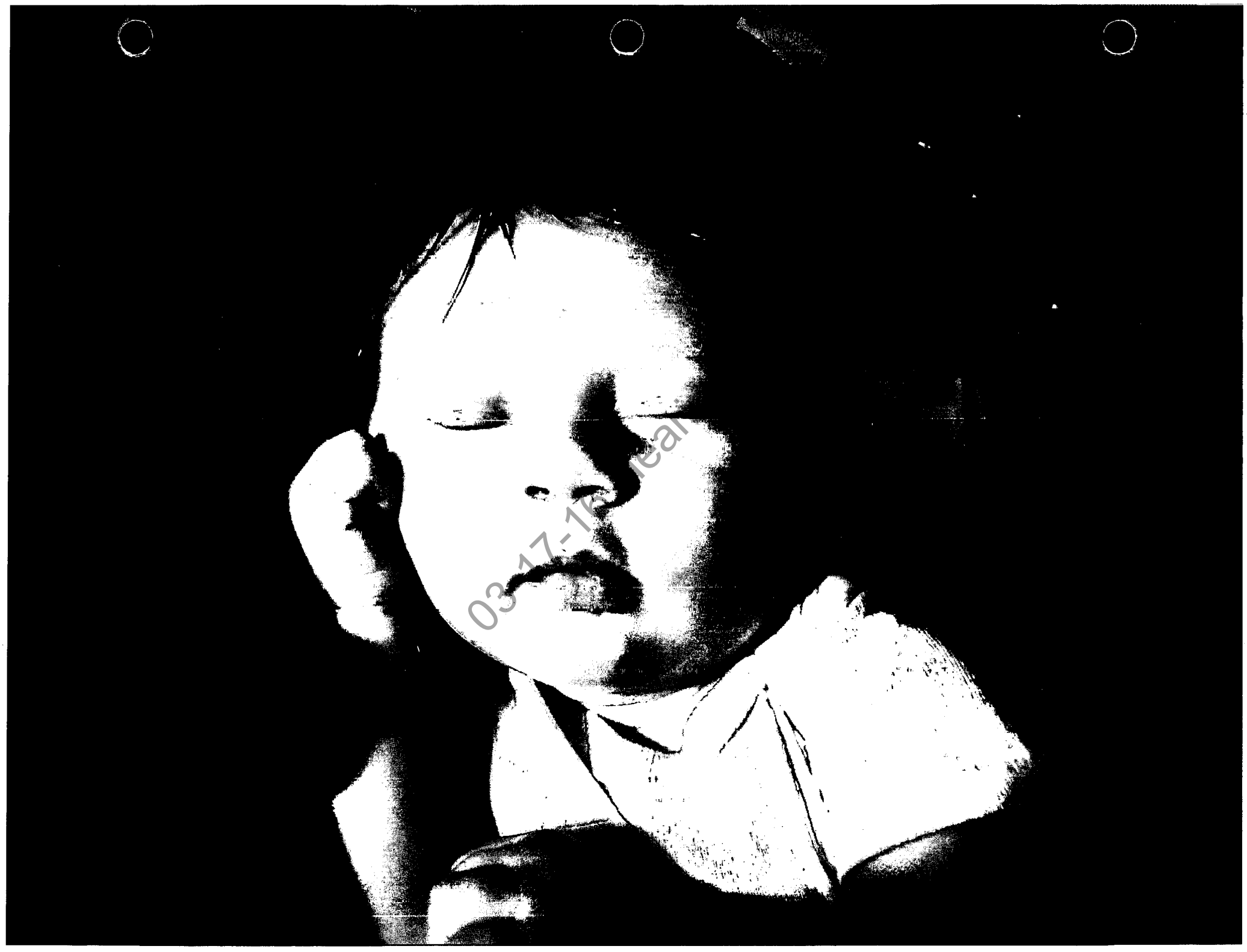
Johan Bakken, MD, PhD
President, IDSA

Carlos del Rio, MD
Chair, HIVMA

Janet Gilsdorf, MD, DSc
President, PIDS

Cc:

Nancy Retzlaff
Eliseo O. Salinas, MD, MSc
Julio Casoy, M.D.



Access to Daraprim (Pyrimethamine)

IDSA, HIVMA, PIDS, NASTAD and RWMPC remain concerned that there has not been an update on the promised price reduction for Daraprim (pyrimethamine) and further that the $750 price per tablet is impacting patient access to this essential treatment. We want to know if you are aware of any access issues to Daraprim (pyrimethamine) since the price increase by Turing Pharmaceuticals. **Turing urges providers and individuals to contact them for assistance accessing the medication either online daraprimdirect.com or by calling call 1-800-222-4991. Please let us know if you, your colleagues or your hospital or clinic has experienced any of the issues below.**

- Had problems accessing therapy during inpatient admissions
- Had to use alternative therapies for treatment of toxoplasmosis or malaria
- Had to prolong hospitalizations until patients could access drug as an outpatient
- Had to switch therapy or had lapses in dosing for ongoing treatment or prophylaxis
- Had difficulties accessing Daraprim (pyrimethamine) through the patient assistance program
- Used the patient assistance program (please let us know how it works)
- Had patients unable to obtain Daraprim (pyrimethamine) through the state AIDS Drug Assistance Program
- Had patients unable to obtain Daraprim (pyrimethamine) through their regular pharmacy
- Worked with a compounding pharmacy to acquire pyrimethamine for patients

Please share your comments with us below or by email. Please note if you post your comments online they will be available for public viewing.

Comments

Tony M says
October 11, 2015 at 6:56 pm

Yes, within the last month I was seeing a child recently diagnosed with toxoplasmosis and was unable to obtain pyrimethamine as all contacted pharmacies had it listed as discontinued by their distributors. I had to change to TMP/SMX despite the fact that data on that therapy in pediatrics is thin.

Reply

E Johnson says
October 11, 2015 at 9:18 pm

I have "suggested" that patients look at Canadian online Pharmacies. I'm told that Daraprim is $145 for 90 25 mg tabs. Other patients tell me that they can get drugs no longer available in USA (e.g. Tetracycline HCL) very reasonably.

Reply

Jason G says
October 12, 2015 at 1:39 pm

I was able to obtain Daraprim last week for a BCBS member, but only after completing a prior auth for a "high dollar exception." I also had to use Community Walgreens Specialty Pharmacy, which had to order it from their central office. I'm not sure what the actual cost was to the payer.

Reply

Mark H says
October 12, 2015 at 2:33 pm

A middle aged man was admitted with a new diagnosis of cerebral toxoplasmosis at our facility. He was ill enough to require discharge to a skilled nursing facility, but we could find no facility that would accept him due to the cost of pyrimethamine and sulfa regimen, thus we were forced to choose an alternate regimen to allow discharge from the hospital.

Reply

MC Bowman says
October 12, 2015 at 8:22 pm

Currently we have two inpatients on pyrimethamine for cerebral toxoplasmosis. We have two days left of pyrimethamine. A single bottle of 100 pills is the smallest the hospital can buy and will thus cost $75,000. Both patient will have to be switched to TMP/SMX

Reply

Jason G says
October 13, 2015 at 10:40 pm

Update: I just learned that my patient's insurance was billed $54,000 for a one month supply of drug.

Reply

J Garcia-Diaz says

October 14, 2015 at 2:22 am

Two patients:

1. toxo retinitis – patient was quoted $26,000.00; upon calling us we tried to change his medications; sulfa allergy and he was desensitized and is on Bactrim now.

2. cerebral toxo – could not get meds refilled (Medicaid) and he is on mepron; renal insufficiency and can't do sulfa agents.

Neither therapy ideal and not first line. In the meantime, the pharmaceutical representative contacted us to introduce himself but requested a meeting first to guide us thru the process.

Reply

Henry F says

October 15, 2015 at 12:39 am

Have two adult patients with AIDS and CNS toxoplasmosis, both foreign born, one of whom is undocumented who is also sulfa allergic, both of whom have ADDP for their HIV medications.

The first patient was able to eventually get pyramethamine through the Daraprim Direct Program via the Walgreens Specialty pharmacy, this process took about 2 weeks and also required her to change her primary pharmacy.

The second patient was more complicated and because of his undocumented status was unable to use the Daraprim Direct Program, he has finally (today) recieved pyramethamine from the Amedra Cares Patient Assistance Program after initial applications were placed a month ago, with subsequent numerous phone calls and many hours of effort from our clinic Pharmacist. He received a temporary 10 day supply from the Walgreens Specialty Pharmacy through his ADDP until the supply could be obtained from Amedra Cares Patient Assistance Program

Reply

David K says

October 19, 2015 at 2:30 pm

Yes, we have had a major issue getting pyrimethamine initially for a pregnant woman here in Birmingham, and then for her baby following delivery.

Reply

Aric says

October 20, 2015 at 6:02 pm

Shortly after the price increase I had to call the pharmacy to switch out pyrimethamine to Bactrim for a patient with ocular toxo. He was Canadian and I suggested that he return to his country to receive proper treatment, but he declined. Since then, I have had difficulty with cycloserine, praziquantel and albendazole with regards to cost.

Reply

Richard R says

October 21, 2015 at 8:29 pm

I am treating a patient with AIDS and CNS toxoplasmosis. As 10 days after diagnosis, we have been unable to obtain pyrimethamine for this patient following hospital discharge.

Reply

Martin Shkreli says

October 23, 2015 at 11:41 pm

Anyone who has difficulty getting Daraprim can call me personally.

Martin Shkreli
CEO
Turing Pharmaceuticals
Office 646-356-5590
Mobile 646-217-2783
Email martin AT turingpharma DOT com

Reply

Annie A says

November 18, 2015 at 2:23 am

I had a significant delay in obtaining pyrimethamine for my patient. She is a renal transplant patient and had toxo in 2011 and also has a sulfa allergy and had been on pyrimethamine+clinda since 2011. One day she stopped getting it from her mail order pharmacy. She is not completely literate and it took her a little while to figure it out and see her output transplant ID doc. The transplant ID doc called Turing during her appt and was told to prescribe the med to the outpt pharmacy of the hospital. Of course, that did not work – so crazy that a Turing person would give wrong information out. So she went to pharmacy and they didn't have it. She didn't let her ID doc know. Then her mental status worsened and she was brought into the hospital. This is where I met her.

Our hospital had a few days supply of pyrimethamine and with receipt of this, her mental status started to improve dramatically. Then 2 days in we were told that our hospital was running out. This was a Saturday. I was the ID consult fellow. So on Saturday, and then on Sunday too, I called every number on Turing's website. Unfortunately I didn't see the blog with Martin Shkreli's number on it till much later otherwise I definitely would have called him. You'd think he'd put his cell phone number on the Turing website which is where physicians are looking for it rather than hidden away on a blog that is difficult to find unless you get a direct email about this issue from IDSA. All numbers stated their open hours which are M-F and left NO way to leave a voicemail. I emailed them. No reply.

By Monday we had run completely out and allergy was consulted to desensitize her to bactrim. FINALLY monday morning I reached a human being and faxed in the form to get the process started to get my patient her med. I labeled it STAT and circled it many times. I called Walgreens specialty pharmacy (the sole distributor to patients) 6 times per day on Monday and Tuesday. They first promised me a 24 hour turnaround bc this was a patient with toxo encephalitis who is allergic to the alternative. They said all my info checked out and they would call the patient to verify. I provided her hospital room number and her cell and explained that she was not able to talk fluently bc she was infected. By Monday night, they had not gotten through the insurance verification process. Really? Pharmacies do this in like 5-10 minutes while you wait! And I am a physician and was saying this was STAT, and it took 24

hours???

Then Tuesday I called again in the morning and early afternoon – insurance hadn't yet been processed. I asked to speak to a supervisor, who said this would be done and the patient would be called within the hour and we would have the med by 6am on Wed AM. Tuesday at 7pm after rounds I called to check in on Walgreens – they hadn't called the patient despite telling me at 1pm they'd do it 'within the hour.' I had already gone to my office, but walked back with them on the line back to my patient's hospital room to make sure that they were able to talk to my patient and not lie to me and just not call her. So they finally connected because I made sure it happened. They said they'd fedex us her med, but then wouldn't tell us when it would arrive.

It finally arrived Wed afternoon. I started the process Sat morning. This is an URGENT need for a patient with encephalitis with unknown sulfa allergy (she was unable to talk w/us – not in record) – I did literally everything anyone could to get her her med as soon as possible, and it took 4.5 days. REALLY? We pay 750 per pill for this, you'd think Walgreens specialty could afford to stay open on the weekend when they are the ONLY distributor of this critical medicine.

The price is outrageous, but the ACCESS is worse! Can you imagine if levophed wasn't available on the weekends? Utter insanity. Pyrimethamine needs to stop being accessed only through one distributor that is closed on the weekends.

Reply

Kyle P says

November 18, 2015 at 6:14 pm

Last month we were treating an AIDS patient for suspected toxo at our facility. Patient was/is noncompliant and was off ARV for some time prior to admission. The patient's hospital course involved a trip to the ICU, intubation for several days, experiencing some delirium post extubation, and plenty of other unpleasant symptoms possibly related to the toxo and an extended hospital/ICU stay.

Our inpatient pharmacy was able to acquire pyrimethamine from the local academic medical center in our area – the cost of acquiring the drug was not exorbitant from my recollection (thankfully). We treated the patient for several days with pyrimethamine and other supportive cares prior to discharge. Our case coordinators worked with the patient's community pharmacy to ensure they had pyrimethamine stocked and ready to be dispensed for the duration of the treatment course. Ample stock was confirmed two days prior to discharge.

The patient was discharged, went to the pharmacy we had been working with, and then suddenly they didn't have stock of the drug. The pharmacist claimed they didn't have appropriate credentials to access the drugs. Bactrim was substituted, which ultimately wasn't tolerated, and another admission was required to treat the patient appropriately.

We are currently investigating what slipped through the cracks at the initial discharge. But there are definitely more issues with accessing and acquiring the drug in recent months, based on our own experience, and based on accounts from colleagues.

Reply

Jon Haas says

November 19, 2015 at 2:19 pm

My name is Jon Haas and I am the Director of Patient Access at Turing Pharmaceuticals. I am solely focused on working to get all patients who need DARAPRIM® (pyrimethamine) quick and affordable access to the drug. Any physician who is having any issue prescribing DARAPRIM, please contact me immediately so that I can work with you to resolve it.

Jon Haas
daraprim AT turingpharma DOT com
Cell: 817-789-0344
Dararaprimdirect.com

Reply

Amy K says
February 4, 2016 at 9:47 pm

I have a patient with AIDS and CNS toxoplasmosis who was initially treated with a sulfa-based regimen on which she developed a severe rash. We switched her to atovaquone+pyrimethamine+leucovorin, and she did well. However, the state ADAP program does not include Daraprim on its formulary because of cost. We investigated both local compounding pharmacies and Imprimis Pharmaceuticals before ADAP granted us a temporary exemption and agreed to pay for one month of Daraprim to give us time to work through the PAP process. Our hospital pharmacist did contact Turing Pharmaceuticals to request access to the PAP and was told that we first had to prove that the patient had no other payor source. Patient will need pyrimethamine for at least three more weeks or until her CD4>200, whichever takes longer.

Our hospital's cost for Daraprim was $1125 per day ($375/pill x 3 pills/day). This cost represents the "50% discount" Turning Pharmaceuticals gives to hospitals. Furthermore, hospitalization was extended by seven days because we could not send the patient home without her pyrimethamine, and it took seven days to obtain the access described above. It is still unclear what will happen when her one-month ADAP supply is gone; Turing still has not confirmed that she will qualify for its PAP.

Reply

Ulrike Buchwald says
March 1, 2016 at 6:41 pm

Please see a very informative article by J. Greene et al in JAMA February 2nd 2016, Volume 315, 5, page 461, on the "Role of the FDA in Affordability of Off-Patent Pharmaceuticals" including a discussion on measures that can be taken to prevent treatment shortages such as in the case of pyrimethamine.

Reply

M Siegel says
March 1, 2016 at 7:18 pm

I had a patient admitted to our for profit hospital for CNS toxoplasmosis. Our pharmacy stated that the pyrimethamine would cost $750 per 25mg pill. Apparently for-profit hospitals are not given any concessions in regards to pricing. Therefore we decided to treated the patient with oral Bactrim DS 2 po tid. The patient did well on this but developed AKI after 7 days of therapy. He was switched over to atovaquone 750mg qid. His repeat MRI

after 2 weeks was unchanged and therefore I contacted Imprimis pharmaceuticals after reading in CID that they were offering pyrimethamine/leucovorin combination pills at $1 per day. The customer support person was extremely helpful and faxed over the order form which I faxed back later that day and my patient had the medication in their possession within 48 hours. I am sure that my patient will show clinical improvement now but the 2 week delay due to the lack of availability of the pyrimethamine was unnecessary if Turing had not made such an aggressive pricing change

Reply

A McLemore, MD says

March 1, 2016 at 11:28 pm

I had to obtain it through a compounding pharmacy. http://imprimispharma.investorroom.com/2015-10-22-Imprimis-Pharmaceuticals-to-Make-Compounded-and-Customizable-Formulation-of-Pyrimethamine-and-Leucovorin-Available-for-Physicians-to-Prescribe-for-their-Patients-as-an-Alternative-to-Daraprim

Reply

D Bullock, MD says

March 10, 2016 at 10:44 pm

I have a sick inpatient, with AIDS, headaches, multiple enhancing cerebellar lesions with elevated pressure, midline shift, left sided weakness and aphasia. He has history of CNS toxoplasmosis, lost to follow up. We have him on trimethoprim-sulfamethoxasole while we wait for pyrimethamine. The cost for one bottle is $75,000 because he is inpatient and has no access to patient assistance (reserved for outpatients).

Reply

Leave a Reply

Your email address will not be published. Required fields are marked *

Comment

Name *

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Website

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ABOUT · E-mail Us
Ph: 703-299-1215 · 1300 Wilson Boulevard, Suite 300, Arlington, VA 22209 · Log in

From: Michael Smith
To: Edwin Urrutia; Michael Smith; Patrick Crutcher
Sent: 10/20/2015 9:09:40 PM
ubject: Conversation with Edwin Urrutia, Michael Smith

Redacted - Not Responsive

Michael Smith 10:18 AM:
24.88 bottles for WG, 54 bottles for ICS (including 29 bottles for WG)
Edwin Urrutia 10:25 AM:
im out
Patrick Crutcher 10:25 AM:
lol
so 53.88 for WG?
Michael Smith 10:26 AM:
nah the 29 part is just a stocking transaction
Patrick Crutcher 10:26 AM:
gotcha
Michael Smith 10:26 AM:
the first 24.88 is the actual dispensed
Edwin Urrutia 10:29 AM:
did tina respond mike?
Michael Smith 10:29 AM:
o
, iaas told me that ics had like 105 on hand when they placed that order yesterday
he was confused why they did it

Redacted - Not Responsive

Redacted - Not Responsive

Redacted - Not Responsive

Edwin Urrutia 2:22 PM:
Shortly after the price increase I had to call the pharmacy to switch out pyrimethamine to Bactrim for a patient with ocular toxo. He was Canadian and I suggested that he return to his country to receive proper treatment, but he declined. Since then, I have had difficulty with cycloserine, praziquantel and albendazole with regards to cost.
latest post of n hivclinician.org
damn even hating on prazi
Michael Smith 2:23 PM:
i think some of these are fake

Redacted - Not Responsive

Redacted - Not Responsive

From: Michael Smith
To: Edwin Urrutia; Michael Smith; Patrick Crutcher
Sent: 10/27/2015 6:37:57 PM
Subject: Conversation with Edwin Urrutia, Michael Smith

Redacted - Not Responsive

Redacted - Not Responsive

2 pts have paid cash for daraprim
rich af
Patrick Crutcher 12:28 PM:
omg
Edwin Urrutia 12:29 PM:
WOW
Michael Smith 12:29 PM:
tina reporting 75% G2N discount
Edwin Urrutia 12:30 PM:
omg
its so bad
Patrick Crutcher 12:31 PM:
time to dip out of 340b
fuck these guys
Michael Smith 12:31 PM:
lol yeah
i told her to start disputing the 340b claims
Patrick Crutcher 12:31 PM:
also, are they verifying some of these 340b claims
hospitals been some motherfuckers about this shit
Michael Smith 12:32 PM:
yeah i think part of the issue is the hospital stocking
and then it is very opaque if they are actually serving 340b pts
Patrick Crutcher 12:32 PM:
yeah and then they give out drug to paying pts at a $1
Edwin Urrutia 12:32 PM:
are we doing a bd meeting?
Michael Smith 12:33 PM:
well i could see them giving it to real pts at 75k
and pocketing it
idc up to you
Patrick Crutcher 12:34 PM:
yeah thats what i meant
paying pts being dudes like us
Edwin Urrutia 12:34 PM:
yeah
Patrick Crutcher 12:34 PM:
not sure these clowns have done anything

Redacted - Not Responsive

Redacted - Not Responsive

Redacted - Not Responsive

Redacted - Not Responsive

Redacted - Not Responsive

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 1:04 PM
To: Martin@retrophin.com
Subject: Re: News

Funny how suddenly in the same week MRK, SNY, ABT are all rumored to sell legacy product portfolios. Fascinating times. All this m+a, asset swapping, divestitures and such should provide years of opportunities for you guys and many others.

I hear you on the pharma mentality - it's ironic how it took two companies - jazz and hznp - the brink of insolvency to decide they should aggressively play the price card. Very different dynamics but basically each company would likely have gone under without those moves, but it took extreme weakness to force that hand. And qcor is obviously a poster-child - for the heat and bad PR they took, didn't work out so badly in the end, did it? Not every deal and every product will work out like these, but for smart managements, that are resourceful and opportunistic, these are exciting times.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:47 AM
To: Dan Wichman
Subject: RE: News

So many legacy assets that people have just forgotten about. This is one of them. It is really a great drug that people need. Docs want more support, awareness, education. It's like Wilson's disease – there hasn't been a Wilson's presentation or symposium in decades thanks to Valeant/Aton/Merck. Docs hate that. Most of them don't know pricing, they just know support—how many reps they see, copays, etc.

The drug companies are afraid. Small ones, big ones, etc. Big price increases are horrifying because most executives overestimate changes in demand. It comes mostly from pharma's history as quasi-consumer products. The next generation of pharma guys (or the smart ones) understand the inelasticity of certain products. The insurers really don't care. They just pass it through and focus on managing care for physician payments and blockbusters. They assume someone will genericize it if it is making too much money, and they're right.

So I don't really think of it the same way as others. I think this deal, if we pull it off, is worth $100m-$200m to our company. We'll see!

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:41 AM
To: Martin Shkreli
Subject: Re: News

Interesting - sounds like a no-lose, to put it mildly. Don't have to run a model on that one this weekend to give you my opinion.

Funny that these small companies still haven't realized you can raise price aggressively and nobody gets too upset? Obviously depends on the product - but I figure this dynamic may not last forever, you need to maximize opportunities while you can. In the real boring spec pharma space I kind of look at hznp vs depo - own and like both companies, have nothing but good things to say about depo - but depo is very cautious and conservative, while hznp says, this price dynamic may not last forever at least on these reformulated pain products, so let's maximize our cash flows now and diversify over time. It's not like people are giving companies gold stars for charging slightly lower prices ("thanks guys for charging 500 an rx not 800") - in that land the generics aren't your competition and don't even try. Sorry that was a quick digression.

Anyway, it's different in orphan land, and probably more sustainable, but seems like at this point these little guys would get the idea that they could push things a bit. How can they ever make money with that model? Bottom line is I won't get too excited but it sounds very intriguing.

Dan Wichman
Partner

[redacted]

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To: Dan Wichman
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The deal we're working on very simple and Manchester like.
We'd pay $1m to acquire a drug called Thiola, which is the only treatment for a rare disease called cystinuria (contrast with RPTP cystinosis – totally different).
The drug does $1.2m in sales. It is woefully underpriced and would not stop selling at orphan prices. With new pricing we estimate sales of $20 to $40 million. Almost 95% EBITDA margins at those prices. Would be an annuity for some time.

A $100m present for you this morning.
All kidding aside, it is still a medium stage negotiation and may not come to fruition. We have a good relationship with the seller and they have a contract sales force which we would use to sell the product, which would add $5m in expenses annually (for them that's another $1m or $2m margin) and a royalty. So it's something of a win-win but a capital W for us and a lowercase for them. It might finish in time to announce Novartis and this one.

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:19 AM
To: Martin Shkreli
Subject: Re: News

I'd say, I'll be happy with the one I know about, but I'm always open to more as long as you guys have the personnel and time and expertise to handle it all.
Glad Steve is on board - seems he knows you well at this point, and you haven't scared him away...

After the Wilson's frustration (which hopefully didn't scar him for life) seems you guys have come a long way.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:14 AM
To: Dan Wichman
Subject: RE: News

Yes, Steve is the best. We really trust and respect each other a huge amount – which is crucial to co-leading a company.

What if I told you we might announce two deals at once?

Hehehehe ☺

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:13 AM
To: Martin Shkreli
Subject: Re: News

Yes fair enough - once this deal closes I'll go back to being less of a pain in the a$$. Sounds good on Steve (a yin and yang perhaps?) and hope the other stuff works out.

Assuming this looks like a done deal this week (knock on wood), I'd love to discuss a little of how you'll convey it to the Street - I'm sure you've spent many hours thinking about that. Will be a fun opportunity. Hopefully your other investors agree the bigger deal is the better deal - but if not they're wrong!

Then I'll go back to leaving you alone and not harassing you semi-hourly - let you do the hard work in creating value.

Dan

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 07:57 AM

To: Dan Wichman
Subject: RE: News

I have to be careful with giving you minute by minute updates on the company ☺

Steve Aselage is joining as President and Chief Operations Officer – you've met him – he's on our Board and as former Chief Business Officer (similar role) at BioMarin I think he will help us not just in commercializing our drugs but also all aspects of the company – he is very savvy politically (has a very different approach from me), well-liked and will just make our company run a lot better across the board.

On Alvin, stay tuned.

From: Dan Wichman [redacted]
Sent: Friday, May 02, 2014 5:41 PM
To: Martin Shkreli
Subject: Re: News

Talked to Barclays - sounds like it's still on track. Fingers crossed for no new roadblocks I'm excited.
Any word on the r+d guy yet?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 02:57 PM
To: Dan Wichman
Subject: RE: News

Yes. It should be a done deal. Never say never though.

From: Dan Wichman [redacted]
Sent: Thursday, May 01, 2014 2:45 PM
To: Martin Shkreli
Subject: RE: News

They've agreed to this? All parties? If so, that is great news, and we'd be very excited. Happy to pick up $10mln in pre-paid royalties to make those clowns happy. The npv is a no-brainer.

Dan Wichman
Partner

[redacted]

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 2:41 PM
To: Dan Wichman
Subject: News

We are doing the entire deal at $190m. You twisted my arm!

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Outlook Mobile Service (Text Messaging)

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 1:32 AM
To: Martin@retrophin.com
Subject: Re: News

Hmm, I'd have questions about, but won't bother. Vnda is annoying but guess their investors would be happy they're squeezing every bit out of this.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:25 PM
To: Dan Wichman
Subject: RE: News

Vanda has a patent they want us to buy and put into orange book. Might actually be an okay deal. Just taking forever.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 9:24 PM
To: Martin Shkreli
Subject: Re: News

Ugh

Dan Wichman
Partner

[redacted]

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:23 PM
To: Dan Wichman
Subject: RE: News

Yep we'll get through it.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 9:07 PM
To: Martin Shkreli
Subject: Re: News

Lemme guess, more nvs roadblocks

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:00 PM
To: Dan Wichman
Subject: RE: News

Never a dull moment!

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 6:29 PM
To: Martin Shkreli
Subject: Re: News

By the way I always appreciate your passion - I know you're in this for the right reasons (helping patients AND value creation), even if twitter is a scary place especially for an unfiltered ceo...anyway, hope NVS is on track and I'll harass barclays about that one.

Talk soon.

Dan

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 04:27 PM
To: Dan Wichman
Subject: RE: News

I don't think it matters. It's one drug out of 10 and doesn't generate revenue. It's important but what one guy says on twitter isn't going to change our fate. If anyone thinks the FDA is sitting there caring what I'm saying, they should sell our stock and move on.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:26 PM
To: Martin Shkreli
Subject: RE: News

It doesn't seem like a simple straightforward issue, but I hear you – it does seem like red tape could be too high in areas where there is no approved drug and the alternative is unavoidable death. We don't want families to have too much hope on something that may not work at all, but obviously the bar should not be super-high in situations such as these. I had thought you guys had respected the FDA's response and were going to address the issues quickly (and I assume you still are), but guess your views on it changed in the last few weeks.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:21 PM
To: Dan Wichman
Subject: RE: News

Sure FDA might say something like that, but it wouldn't be true and telling a family what they can or can't do to save their dying kid is crazy. The CEO of RARE believes the same thing, he is basically on a crusade against FDA on this very topic.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:17 PM
To: Martin Shkreli
Subject: RE: News

Ok, that sounds good, but don't you think FDA would also say, Retrophin didn't do a great job with the IND for xx and xx reasons, and sponsors owe it to the patients to do pristine jobs with filings such as this? Especially when you're putting a new drug into humans for the first time ever? Or am I crazy. Anyway, the tweeting I'm sure doesn't change much either way, I don't mind cringing now and then as long as you're doing all the right stuff behind the scenes and my confidence is high you're gonna create tons of value, which it is.

Though I must admit beyond the FDA thing, not sure why you need to ever respond to these idiotic retail guys who criticize you – who cares!

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:12 PM

To: Dan Wichman
Subject: RE: News

Sure, mobilizing people to get things to change. We think we could get the decision reversed. The FDA needs new compassionate use laws. Dying kids, etc. It's terrible. AIDS activists didn't let it go quietly into the night and companies were too embarrassed to say anything. The FDA isn't a judgmental crazy place, they use facts and come to decisions reasonably well. The idea they have orphan in the GI division is laughable and sad for people who have diseases like PKAN. We'll see if the activism works but I'm told >1,000 people have written the FDA and 7 senators have called them.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:08 PM
To: Martin Shkreli
Subject: RE: News

But is there anything to be gained? I know you're not into politics and diplomacy but not sure how it can possibly help you guys.
Not a big issue, but was pointed out to me by another investor who was turned off by it – I don't think it matters a huge amount but I did cringe reading those comments.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:05 PM
To: Dan Wichman
Subject: RE: News

don't think it makes a difference. The place turns over so fast and I have great relationships with lots of the key people.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 3:11 PM
To: Martin Shkreli
Subject: RE: News

Hey, hope weekend was good. Hadn't seen it but was brought to my attention by another investor – do you think it's a good idea to bash FDA on twitter? Seems like there isn't much to gain there unless you have some motive I don't know about. Am I crazy?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 8:48 AM
To: Dan Wichman
Subject: RE: News

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To: Martin Shkreli
Subject: Re: News

I'd say, I'll be happy with the one I know about, but I'm always open to more as long as you guys have the personnel and time and expertise to handle it all.
Glad Steve is on board - seems he knows you well at this point, and you haven't scared him away...
After the Wilson's frustration (which hopefully didn't scar him for life) seems you guys have come a long way.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:14 AM
To: Dan Wichman
Subject: RE: News

Yes, Steve is the best. We really trust and respect each other a huge amount – which is crucial to co-leading a company.

What if I told you we might announce two deals at once?

Hehehehe ☺

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Sent: Saturday, May 03, 2014 8:13 AM
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Yes fair enough - once this deal closes I'll go back to being less of a pain in the a$$. Sounds good on Steve (a yin and yang perhaps?) and hope the other stuff works out.

Assuming this looks like a done deal this week (knock on wood), I'd love to discuss a little of how you'll convey it to the Street - I'm sure you've spent many hours thinking about that. Will be a fun opportunity. Hopefully your other investors agree the bigger deal is the better deal - but if not they're wrong!

Then I'll go back to leaving you alone and not harassing you semi-hourly - let you do the hard work in creating value.

Dan

Dan Wichman
Partner

[redacted]

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Subject: RE: News

I have to be careful with giving you minute by minute updates on the company ☺

Steve Aselage is joining as President and Chief Operations Officer – you've met him – he's on our Board and as former Chief Business Officer (similar role) at BioMarin I think he will help us not just in commercializing our drugs but also all aspects of the company – he is very savvy politically (has a very different approach from me), well-liked and will just make our company run a lot better across the board.

On Alvin, stay tuned.

From: Dan Wichman [redacted]
Sent: Friday, May 02, 2014 5:41 PM
To: Martin Shkreli
Subject: Re: News

Talked to Barclays - sounds like it's still on track. Fingers crossed for no new roadblocks I'm excited.
Any word on the r+d guy yet?

Dan Wichman
Partner

[redacted]

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 02:57 PM
To: Dan Wichman
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Yes. It should be a done deal. Never say never though.

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[redacted]

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We are doing the entire deal at $190m. You twisted my arm!

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From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 3:44 PM
To: Martin Shkreli
Subject: RE: News

Music to my ears. Still hope this deal gets done – don't wanna have to explain another one internally – but yeah I'm confident you can find something.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 11:38 AM
To: Dan Wichman
Subject: RE: News

We'll see. I am confident, plus I have other big value-add deals. I am worry-free and carefree right now. You guys can do all the worrying ☺

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 11:37 AM
To: Martin Shkreli
Subject: RE: News

Man what a painful process. Rivaling Wilson's isn't it. You get this deal done, remove cash overhang, lay out the accretion, stock goes back to 20…which is why it probably won't happen the way things are going for us these days.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 11:21 AM
To: Dan Wichman
Subject: RE: News

Still waiting!

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 11:09 AM
To: Martin Shkreli
Subject: RE: News

Hey man – any update on things? Kevin asking. I'm assuming and bracing for the worst...but hopeful I'm too cynical.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 10:50 AM
To: Dan Wichman
Subject: RE: News

Baker Brothers might help. Who knows. We are committed to success with this drug. Worst case we can just buy Fanapt ☺

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 10:44 AM
To: Martin Shkreli
Subject: Re: News

I'd volunteer to mediate but not sure Mihalis is a huge fan of mine. But man I really hope they don't muck this up - have very high hopes here.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 09:21 AM
To: Dan Wichman
Subject: RE: News

I think they want to sue Novartis and get a big settlement – I'm sure you've seen some of these 'commercial deals go wrong' with big pharma, and the big pharma pays $25 - $100m in a settlement to "get out". Like Pfizer with Exubera, even Merck has done it I think.

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 9:17 AM
To: Martin Shkreli
Subject: Re: News

Seems crazy to suddenly want to make that part of the deal. Can't you agree to look at after? Nvs sure as heck won't do it so maybe here you actually have some leverage? If they're getting royalties upfront, seems they want this to happen - do they yet appreciate you're not going to do a worse job than novartis on this?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 09:08 AM
To: Dan Wichman
Subject: RE: News

It sounds like they really want to make Fanapt last longer, which is actually really smart, and probably appreciated by all of us. If Fanapt lasts 5 more years, great. Their plan is a little nuts, which as you know, requires a lot of clinical work and risk and may not be worth the expense to us but they'd be very happy if someone did it.

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 9:02 AM
To: Martin Shkreli
Subject: RE: News

Getting ridiculous. I appreciate them trying to get some non-dilutive financing out of it, if I were a holder I'd like that, but come on. Enough is enough! I assume this is something that had never even come up until now. I don't know the latest details but Mihalis is now pissing me off.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 9:00 AM
To: Dan Wichman
Subject: RE: News

Yeah especially given we have 2 of the 3 consents. They are the loan holdout.

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 6:39 AM
To: Martin Shkreli
Subject: Re: News

Is it me or do they keep moving the goalposts? Doesn't seem like good faith business. Guess they could care less if deal happens or not so they try to milk it for all they can, but at a certain point it becomes ridiculous. Patent deals seem like you could work with them on later.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:25 PM
To: Dan Wichman
Subject: RE: News

Vanda has a patent they want us to buy and put into orange book. Might actually be an okay deal. Just taking forever.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 9:24 PM
To: Martin Shkreli
Subject: Re: News

Ugh

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:23 PM
To: Dan Wichman
Subject: RE: News

Yep we'll get through it.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 9:07 PM
To: Martin Shkreli
Subject: Re: News

Lemme guess, more nvs roadblocks

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:00 PM
To: Dan Wichman
Subject: RE: News

Never a dull moment!

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 6:29 PM
To: Martin Shkreli
Subject: Re: News

By the way I always appreciate your passion - I know you're in this for the right reasons (helping patients AND value creation), even if twitter is a scary place especially for an unfiltered ceo...anyway, hope NVS is on track and I'll harass barclays about that one.

Talk soon.

Dan

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 04:27 PM
To: Dan Wichman
Subject: RE: News

I don't think it matters. It's one drug out of 10 and doesn't generate revenue. It's important but what one guy says on twitter isn't going to change our fate. If anyone thinks the FDA is sitting there caring what I'm saying, they should sell our stock and move on.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:26 PM
To: Martin Shkreli
Subject: RE: News

It doesn't seem like a simple straightforward issue, but I hear you – it does seem like red tape could be too high in areas where there is no approved drug and the alternative is unavoidable death. We don't want families to have too much hope on something that may not work at all, but obviously the bar should not be super-high in situations such as these. I had thought you guys had respected the FDA's response and were going to address the issues quickly (and I assume you still are), but guess your views on it changed in the last few weeks.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:21 PM
To: Dan Wichman
Subject: RE: News

Sure FDA might say something like that, but it wouldn't be true and telling a family what they can or can't do to save their dying kid is crazy. The CEO of RARE believes the same thing, he is basically on a crusade against FDA on this very topic.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:17 PM
To: Martin Shkreli
Subject: RE: News

Ok, that sounds good, but don't you think FDA would also say, Retrophin didn't do a great job with the IND for xx and xx reasons, and sponsors owe it to the patients to do pristine jobs with filings such as this? Especially when you're putting a new drug into humans for the first time ever? Or am I crazy. Anyway, the tweeting I'm sure doesn't change much either way, I don't mind cringing now and then as long as you're doing all the right stuff behind the scenes and my confidence is high you're gonna create tons of value, which it is.

Though I must admit beyond the FDA thing, not sure why you need to ever respond to these idiotic retail guys who criticize you – who cares!

Dan Wichman
Partner

[redacted]

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:12 PM
To: Dan Wichman
Subject: RE: News

Sure, mobilizing people to get things to change. We think we could get the decision reversed. The FDA needs new compassionate use laws. Dying kids, etc. It's terrible. AIDS activists didn't let it go quietly into the night and companies were too embarrassed to say anything. The FDA isn't a judgmental crazy place, they use facts and come to decisions reasonably well. The idea they have orphan in the GI division is laughable and sad for people who have diseases like PKAN. We'll see if the activism works but I'm told >1,000 people have written the FDA and 7 senators have called them.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:08 PM
To: Martin Shkreli
Subject: RE: News

But is there anything to be gained? I know you're not into politics and diplomacy but not sure how it can possibly help you guys.
Not a big issue, but was pointed out to me by another investor who was turned off by it – I don't think it matters a huge amount but I did cringe reading those comments.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:05 PM
To: Dan Wichman
Subject: RE: News

don't think it makes a difference. The place turns over so fast and I have great relationships with lots of the key people.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 3:11 PM
To: Martin Shkreli
Subject: RE: News

Hey, hope weekend was good. Hadn't seen it but was brought to my attention by another investor – do you think it's a good idea to bash FDA on twitter? Seems like there isn't much to gain there unless you have some motive I don't know about. Am I crazy?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 8:48 AM
To: Dan Wichman
Subject: RE: News

So many legacy assets that people have just forgotten about. This is one of them. It is really a great drug that people need. Docs want more support, awareness, education. It's like Wilson's disease – there hasn't been a Wilson's presentation or symposium in decades thanks to Valeant/Aton/Merck. Docs hate that. Most of them don't know pricing, they just know support—how many reps they see, copays, etc.

The drug companies are afraid. Small ones, big ones, etc. Big price increases are horrifying because most executives overestimate changes in demand. It comes mostly from pharma's history as quasi-consumer products. The next generation of pharma guys (or the smart ones) understand the inelasticity of certain products. The insurers really don't care. They just pass it through and focus on managing care for physician payments and blockbusters. They assume someone will genericize it if it is making too much money, and they're right.

So I don't real y think of it the same way as others. I think this deal, if we pull it off, is worth $100m-$200m to our company. We'll see!

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:41 AM
To: Martin Shkreli
Subject: Re: News

Interesting - sounds like a no-lose, to put it mildly. Don't have to run a model on that one this weekend to give you my opinion.

Funny that these small companies still haven't realized you can raise price aggressively and nobody gets too upset? Obviously depends on the product - but I figure this dynamic may not last forever, you need to maximize opportunities while you can. In the real boring spec pharma space I kind of look at hznp vs depo - own and like both companies, have nothing but good things to say about depo - but depo is very cautious and conservative, while hznp says, this price dynamic may not last forever at least on these reformulated pain products, so let's maximize our cash flows now and diversify over time. It's not like people are giving companies gold stars for charging slightly lower prices ("thanks guys for charging 500 an rx not 800") - in that land the generics aren't your competition and don't even try. Sorry that was a quick digression.

Anyway, it's different in orphan land, and probably more sustainable, but seems like at this point these little guys would get the idea that they could push things a bit. How can they ever make money with that model? Bottom line is I won't get too excited but it sounds very intriguing.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:23 AM
To: Dan Wichman
Subject: RE: News

The deal we're working on very simple and Manchester like.
We'd pay $1m to acquire a drug called Thiola, which is the only treatment for a rare disease called cystinuria (contrast with RPTP cystinosis – totally different).
The drug does $1.2m in sales. It is woefully underpriced and would not stop selling at orphan prices. With new pricing we estimate sales of $20 to $40 million. Almost 95% EBITDA margins at those prices. Would be an annuity for some time.

A $100m present for you this morning.
All kidding aside, it is still a medium stage negotiation and may not come to fruition. We have a good relationship with the seller and they have a contract sales force which we would use to sell the product, which would add $5m in expenses annually (for them that's another $1m or $2m margin) and a royalty. So it's something of a win-win but a capital W for us and a lowercase for them. It might finish in t me to announce Novartis and this one.

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:19 AM
To: Martin Shkreli
Subject: Re: News

I'd say, I'll be happy with the one I know about, but I'm always open to more as long as you guys have the personnel and time and expertise to handle it all.
Glad Steve is on board - seems he knows you well at this point, and you haven't scared him away...
After the Wilson's frustration (which hopefully didn't scar him for life) seems you guys have come a long way.

Dan Wichman
Partner

[redacted]

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Then I'll go back to leaving you alone and not harassing you semi-hourly - let you do the hard work in creating value.

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Dan Wichman
Partner

[redacted]

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I have to be careful with giving you minute by minute updates on the company ☺

Steve Aselage is joining as President and Chief Operations Officer – you've met him – he's on our Board and as former Chief Business Officer (similar role) at BioMarin I think he will help us not just in commercializing our drugs but also all aspects of the company – he is very savvy politically (has a very different approach from me), well-liked and will just make our company run a lot better across the board.

On Alvin, stay tuned.

From: Dan Wichman [redacted]
Sent: Friday, May 02, 2014 5:41 PM
To: Martin Shkreli
Subject: Re: News

Talked to Barclays - sounds like it's still on track. Fingers crossed for no new roadblocks I'm excited.
Any word on the r+d guy yet?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 02:57 PM
To: Dan Wichman
Subject: RE: News

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To: Martin Shkreli
Subject: RE: News

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Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 2:41 PM
To: Dan Wichman
Subject: News

We are doing the entire deal at $190m. You twisted my arm!

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From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 6:46 PM
To: Martin Shkreli
Subject: RE: News

You know that's not what I want – I want NVS done here and the convert priced tomorrow. We'll all be very happy.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 2:43 PM
To: Dan Wichman
Subject: RE: News

We can always do the convert at a 50% premium if you want ☺☺

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 2:42 PM
To: Martin Shkreli
Subject: RE: News

Nor do i. interesting dynamic now because you and probably most of your bullish friends, like us, are restricted, so some small guys and retail guys playing around now. Whatever, it's fine, hopefully NVS gets done and I'll end up being happy with where the stock price is now (as will you to some degree if you're able to participate).

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 2:40 PM
To: Dan Wichman
Subject: RE: News

Would try to announce a small acquisition with any financing. Otherwise I actually think we can grind out the Manchester payments or do a tiny convert. I really don't like needless dilution.

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 2:38 PM
To: Martin Shkreli
Subject: RE: News

I hear you, but to say stock price should be down at Manchester levels is a bit overdone. If this doesn't happen, will you still a convert to pay Manchester or look at different financing.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 2:36 PM
To: Dan Wichman
Subject: RE: News

Exactly, it will be over soon one way or another. The cost of capital is a small part in my eyes given the return. Also if Vanda doesn't want to play ball, I can buy Thiola (which should be NPV+100 to 200m), announce two senior exec hires, start PKAN trial, print positive EPS and buy Clozaril down the road for a good price with low CoC. I'm cool with that. There is no benefit to a too high stock price, as Buffett says "it's like wanting an egg in your beer".

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 2:34 PM
To: Martin Shkreli
Subject: RE: News

You must be slightly irritated that the deal continues to get more expensive by the minute...I'm not as long as we get our full allocation in the convert. But I am annoyed we can't buy on the open market right now. Such is life. Can't drag out forever can it.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 11:38 AM
To: Dan Wichman
Subject: RE: News

We'll see. I am confident, plus I have other big value-add deals. I am worry-free and carefree right now. You guys can do all the worrying ☺

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 11:37 AM
To: Martin Shkreli
Subject: RE: News

Man what a painful process. Rivaling Wilson's isn't it. You get this deal done, remove cash overhang, lay out the accretion, stock goes back to 20...which is why it probably won't happen the way things are going for us these days.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 11:21 AM
To: Dan Wichman
Subject: RE: News

Still waiting!

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 11:09 AM
To: Martin Shkreli
Subject: RE: News

Hey man – any update on things? Kevin asking. I'm assuming and bracing for the worst...but hopeful I'm too cynical.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 10:50 AM
To: Dan Wichman
Subject: RE: News

Baker Brothers might help. Who knows. We are committed to success with this drug. Worst case we can just buy Fanapt ☺

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 10:44 AM
To: Martin Shkreli
Subject: Re: News

I'd volunteer to mediate but not sure Mihalis is a huge fan of mine. But man I really hope they don't muck this up - have very high hopes here.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 09:21 AM
To: Dan Wichman
Subject: RE: News

I think they want to sue Novartis and get a big settlement – I'm sure you've seen some of these 'commercial deals go wrong' with big pharma, and the big pharma pays $25 - $100m in a settlement to "get out". Like Pfizer with Exubera, even Merck has done it I think.

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 9:17 AM
To: Martin Shkreli
Subject: Re: News

Seems crazy to suddenly want to make that part of the deal. Can't you agree to look at after? Nvs sure as heck won't do it so maybe here you actually have some leverage? If they're getting royalties upfront, seems they want this to happen - do they yet appreciate you're not going to do a worse job than novartis on this?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 09:08 AM
To: Dan Wichman
Subject: RE: News

It sounds like they really want to make Fanapt last longer, which is actually really smart, and probably appreciated by all of us. If Fanapt lasts 5 more years, great. Their plan is a little nuts, which as you know, requires a lot of clinical work and risk and may not be worth the expense to us but they'd be very happy if someone did it.

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 9:02 AM
To: Martin Shkreli
Subject: RE: News

Getting ridiculous. I appreciate them trying to get some non-dilutive financing out of it, if I were a holder I'd like that, but come on. Enough is enough! I assume this is something that had never even come up until now. I don't know the latest details but Mihalis is now pissing me off.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 9:00 AM
To: Dan Wichman
Subject: RE: News

Yeah especially given we have 2 of the 3 consents. They are the loan holdout.

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 6:39 AM
To: Martin Shkreli
Subject: Re: News

Is it me or do they keep moving the goalposts? Doesn't seem like good faith business. Guess they could care less if deal happens or not so they try to milk it for all they can, but at a certain point it becomes ridiculous. Patent deals seem like you could work with them on later.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:25 PM
To: Dan Wichman

Subject: RE: News

Vanda has a patent they want us to buy and put into orange book. Might actually be an okay deal. Just taking forever.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 9:24 PM
To: Martin Shkreli
Subject: Re: News

Ugh

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:23 PM
To: Dan Wichman
Subject: RE: News

Yep we'll get through it.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 9:07 PM
To: Martin Shkreli
Subject: Re: News

Lemme guess, more nvs roadblocks

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:00 PM
To: Dan Wichman
Subject: RE: News

Never a dull moment!

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 6:29 PM
To: Martin Shkreli
Subject: Re: News

By the way I always appreciate your passion - I know you're in this for the right reasons (helping patients AND value creation), even if twitter is a scary place especially for an unf ltered ceo...anyway, hope NVS is on track and I'll harass barclays about that one.

Talk soon.

Dan

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 04:27 PM
To: Dan Wichman
Subject: RE: News

I don't think it matters. It's one drug out of 10 and doesn't generate revenue. It's important but what one guy says on twitter isn't going to change our fate. If anyone thinks the FDA is sitting there caring what I'm saying, they should sell our stock and move on.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:26 PM
To: Martin Shkreli
Subject: RE: News

It doesn't seem like a simple straightforward issue, but I hear you – it does seem like red tape could be too high in areas where there is no approved drug and the alternative is unavoidable death. We don't want families to have too much hope on something that may not work at all, but obviously the bar should not be super-high in situations such as these. I had thought you guys had respected the FDA's response and were going to address the issues quickly (and I assume you still are), but guess your views on it changed in the last few weeks.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:21 PM
To: Dan Wichman
Subject: RE: News

Sure FDA might say something like that, but it wouldn't be true and telling a family what they can or can't do to save their dying kid is crazy. The CEO of RARE believes the same thing, he is basically on a crusade against FDA on this very topic.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:17 PM
To: Martin Shkreli
Subject: RE: News

Ok, that sounds good, but don't you think FDA would also say, Retrophin didn't do a great job with the IND for xx and xx reasons, and sponsors owe it to the patients to do pristine jobs with filings such as this? Especially when you're putting a new drug into humans for the first time ever? Or am I crazy. Anyway, the tweeting I'm sure doesn't change much either way, I don't mind cringing now and then as long as you're doing all the right stuff behind the scenes and my confidence is high you're gonna create tons of value, which it is.

Though I must admit beyond the FDA thing, not sure why you need to ever respond to these idiotic retail guys who criticize you – who cares!

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:12 PM
To: Dan Wichman
Subject: RE: News

Sure, mobilizing people to get things to change. We think we could get the decision reversed. The FDA needs new compassionate use laws. Dying kids, etc. It's terrible. AIDS activists didn't let it go quietly into the night and companies were too embarrassed to say anything. The FDA isn't a judgmental crazy place, they use facts and come to decisions reasonably well. The idea they have orphan in the GI division is laughable and sad for people who have diseases like PKAN. We'll see if the activism works but I'm told >1,000 people have written the FDA and 7 senators have called them.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:08 PM
To: Martin Shkreli
Subject: RE: News

But is there anything to be gained? I know you're not into politics and diplomacy but not sure how it can possibly help you guys.
Not a big issue, but was pointed out to me by another investor who was turned off by it – I don't think it matters a huge amount but I did cringe reading those comments.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:05 PM
To: Dan Wichman
Subject: RE: News

don't think it makes a difference. The place turns over so fast and I have great relationships with lots of the key people.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 3:11 PM
To: Martin Shkreli
Subject: RE: News

Hey, hope weekend was good. Hadn't seen it but was brought to my attention by another investor – do you think it's a good idea to bash FDA on twitter? Seems like there isn't much to gain there unless you have some motive I don't know about. Am I crazy?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 8:48 AM
To: Dan Wichman
Subject: RE: News

So many legacy assets that people have just forgotten about. This is one of them. It is really a great drug that people need. Docs want more support, awareness, education. It's like Wilson's disease – there hasn't been a Wilson's presentation or symposium in decades thanks to Valeant/Aton/Merck. Docs hate that. Most of them don't know pricing, they just know support—how many reps they see, copays, etc.

The drug companies are afraid. Small ones, big ones, etc. Big price increases are horrifying because most executives overestimate changes in demand. It comes mostly from pharma's history as quasi-consumer products. The next generation of pharma guys (or the smart ones) understand the inelasticity of certain products. The insurers really don't care. They just pass it through and focus on managing care for physician payments and blockbusters. They assume someone will genericize it if it is making too much money, and they're right.

So I don't really think of it the same way as others. I think this deal, if we pull it off, is worth $100m-$200m to our company. We'll see!

From: Dan Wichman[redacted]
Sent: Saturday, May 03, 2014 8:41 AM
To: Martin Shkreli
Subject: Re: News

Interesting - sounds like a no-lose, to put it mildly. Don't have to run a model on that one this weekend to give you my opinion.

Funny that these small companies still haven't realized you can raise price aggressively and nobody gets too upset? Obviously depends on the product - but I figure this dynamic may not last forever, you need to maximize opportunities while you can. In the real boring spec pharma space I kind of look at hznp vs depo - own and like both companies, have nothing but good things to say about depo - but depo is very cautious and conservative, while hznp says, this price dynamic may not last forever at least on these reformulated pain products, so let's maximize our cash flows now and diversify over time. It's not like people are giving companies gold stars for charging slightly lower prices ("thanks guys for charging 500 an rx not 800") - in that land the generics aren't your competition and don't even try. Sorry that was a quick digression.

Anyway, it's different in orphan land, and probably more sustainable, but seems like at this point these little guys would get the idea that they could push things a bit. How can they ever make money with that model? Bottom line is I won't get too excited but it sounds very intriguing.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:23 AM
To: Dan Wichman
Subject: RE: News

The deal we're working on very simple and Manchester like.
We'd pay $1m to acquire a drug called Thiola, which is the only treatment for a rare disease called cystinuria (contrast with RPTP cystinosis – totally different).
The drug does $1.2m in sales. It is woefully underpriced and would not stop selling at orphan prices. With new pricing we estimate sales of $20 to $40 million. Almost 95% EBITDA margins at those prices. Would be an annuity for some time.

A $100m present for you this morning.
All kidding aside, it is still a medium stage negotiation and may not come to fruition. We have a good relationship with the seller and they have a contract sales force which we would use to sell the product, which would add $5m in expenses annually (for them that's another $1m or $2m margin) and a royalty. So it's something of a win-win but a capital W for us and a lowercase for them. It might finish in time to announce Novartis and this one.

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:19 AM
To: Martin Shkreli
Subject: Re: News

I'd say, I'll be happy with the one I know about, but I'm always open to more as long as you guys have the personnel and time and expertise to handle it all.
Glad Steve is on board - seems he knows you well at this point, and you haven't scared him away...
After the Wilson's frustration (which hopefully didn't scar him for life) seems you guys have come a long way.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:14 AM
To: Dan Wichman
Subject: RE: News

Yes, Steve is the best. We really trust and respect each other a huge amount – which is crucial to co-leading a company.

What if I told you we might announce two deals at once?

Hehehehe ☺

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:13 AM
To: Martin Shkreli
Subject: Re: News

Yes fair enough - once this deal closes I'll go back to being less of a pain in the a$$. Sounds good on Steve (a yin and yang perhaps?) and hope the other stuff works out.

Assuming this looks like a done deal this week (knock on wood), I'd love to discuss a little of how you'll convey it to the Street - I'm sure you've spent many hours thinking about that. Will be a fun opportunity. Hopefully your other investors agree the bigger deal is the better deal - but if not they're wrong!

Then I'll go back to leaving you alone and not harassing you semi-hourly - let you do the hard work in creating value.

Dan

Dan Wichman
Partner

[redacted]

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 07:57 AM
To: Dan Wichman
Subject: RE: News

I have to be careful with giving you minute by minute updates on the company ☺

Steve Aselage is joining as President and Chief Operations Officer – you've met him – he's on our Board and as former Chief Business Officer (similar role) at BioMarin I think he will help us not just in commercializing our drugs but also all aspects of the company – he is very savvy politically (has a very different approach from me), well-liked and will just make our company run a lot better across the board.

On Alvin, stay tuned.

From: Dan Wichman [redacted]
Sent: Friday, May 02, 2014 5:41 PM
To: Martin Shkreli
Subject: Re: News

Talked to Barclays - sounds like it's still on track. Fingers crossed for no new roadblocks I'm excited.
Any word on the r+d guy yet?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 02:57 PM
To: Dan Wichman
Subject: RE: News

Yes. It should be a done deal. Never say never though.

From: Dan Wichman [redacted]
Sent: Thursday, May 01, 2014 2:45 PM
To: Martin Shkreli
Subject: RE: News

They've agreed to this? All parties? If so, that is great news, and we'd be very excited. Happy to pick up $10mln in pre-paid royalties to make those clowns happy. The npv is a no-brainer.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 2:41 PM
To: Dan Wichman
Subject: News

We are doing the entire deal at $190m. You twisted my arm!

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From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 6:50 PM
To: Martin Shkreli
Subject: RE: News

And I won't ask about the two exec comment...ie head of R&D. See, I'm behaving.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 2:43 PM
To: Dan Wichman
Subject: RE: News

We can always do the convert at a 50% premium if you want ☺☺

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 2:42 PM
To: Martin Shkreli
Subject: RE: News

Nor do i. interesting dynamic now because you and probably most of your bullish friends, like us, are restricted, so some small guys and retail guys playing around now. Whatever, it's fine, hopefully NVS gets done and I'll end up being happy with where the stock price is now (as will you to some degree if you're able to participate).

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 2:40 PM
To: Dan Wichman
Subject: RE: News

Would try to announce a small acquisition with any financing. Otherwise I actually think we can grind out the Manchester payments or do a tiny convert. I really don't like needless dilution.

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 2:38 PM
To: Martin Shkreli
Subject: RE: News

I hear you, but to say stock price should be down at Manchester levels is a bit overdone. If this doesn't happen, will you still a convert to pay Manchester or look at different financing.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 2:36 PM
To: Dan Wichman
Subject: RE: News

Exactly, it will be over soon one way or another. The cost of capital is a small part in my eyes given the return. Also if Vanda doesn't want to play ball, I can buy Thiola (which should be NPV+100 to 200m), announce two senior exec hires, start PKAN trial, print positive EPS and buy Clozaril down the road for a good price with low CoC. I'm cool with that. There is no benefit to a too high stock price, as Buffett says "it's like wanting an egg in your beer".

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 2:34 PM
To: Martin Shkreli
Subject: RE: News

You must be slightly irritated that the deal continues to get more expensive by the minute...I'm not as long as we get our full allocation in the convert. But I am annoyed we can't buy on the open market right now. Such is life. Can't drag out forever can it.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 11:38 AM
To: Dan Wichman
Subject: RE: News

We'll see. I am confident, plus I have other big value-add deals. I am worry-free and carefree right now. You guys can do all the worrying ☺

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 11:37 AM
To: Martin Shkreli
Subject: RE: News

Man what a painful process. Rivaling Wilson's isn't it. You get this deal done, remove cash overhang, lay out the accretion, stock goes back to 20...which is why it probably won't happen the way things are going for us these days.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Wednesday, May 07, 2014 11:21 AM
To: Dan Wichman
Subject: RE: News

Still waiting!

From: Dan Wichman [redacted]
Sent: Wednesday, May 07, 2014 11:09 AM
To: Martin Shkreli
Subject: RE: News

Hey man – any update on things? Kevin asking. I'm assuming and bracing for the worst...but hopeful I'm too cynical.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 10:50 AM
To: Dan Wichman
Subject: RE: News

Baker Brothers might help. Who knows. We are committed to success with this drug. Worst case we can just buy Fanapt ☺

From: Dan Wichman[redacted]
Sent: Tuesday, May 06, 2014 10:44 AM
To: Martin Shkreli
Subject: Re: News

I'd volunteer to mediate but not sure Mihalis is a huge fan of mine. But man I really hope they don't muck this up - have very high hopes here.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 09:21 AM
To: Dan Wichman
Subject: RE: News

I think they want to sue Novartis and get a big settlement – I'm sure you've seen some of these 'commercial deals go wrong' with big pharma, and the big pharma pays $25 - $100m in a settlement to "get out". Like Pfizer with Exubera, even Merck has done it I think.

From: Dan Wichman[redacted]
Sent: Tuesday, May 06, 2014 9:17 AM
To: Martin Shkreli
Subject: Re: News

Seems crazy to suddenly want to make that part of the deal. Can't you agree to look at after? Nvs sure as heck won't do it so maybe here you actually have some leverage? If they're getting royalties upfront, seems they want this to happen - do they yet appreciate you're not going to do a worse job than novartis on this?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 09:08 AM
To: Dan Wichman
Subject: RE: News

It sounds like they really want to make Fanapt last longer, which is actually really smart, and probably appreciated by all of us. If Fanapt lasts 5 more years, great. Their plan is a little nuts, which as you know, requires a lot of clinical work and risk and may not be worth the expense to us but they'd be very happy if someone did it.

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 9:02 AM
To: Martin Shkreli
Subject: RE: News

Getting ridiculous. I appreciate them trying to get some non-dilutive financing out of it, if I were a holder I'd like that, but come on. Enough is enough! I assume this is something that had never even come up until now. I don't know the latest details but Mihalis is now pissing me off.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Tuesday, May 06, 2014 9:00 AM
To: Dan Wichman
Subject: RE: News

Yeah especially given we have 2 of the 3 consents. They are the loan holdout.

From: Dan Wichman [redacted]
Sent: Tuesday, May 06, 2014 6:39 AM
To: Martin Shkreli
Subject: Re: News

Is it me or do they keep moving the goalposts? Doesn't seem like good faith business. Guess they could care less if deal happens or not so they try to milk it for all they can, but at a certain point it becomes ridiculous. Patent deals seem like you could work with them on later.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:25 PM
To: Dan Wichman

Subject: RE: News

Vanda has a patent they want us to buy and put into orange book. Might actually be an okay deal. Just taking forever.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 9:24 PM
To: Martin Shkreli
Subject: Re: News

Ugh

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:23 PM
To: Dan Wichman
Subject: RE: News

Yep we'll get through it.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 9:07 PM
To: Martin Shkreli
Subject: Re: News

Lemme guess, more nvs roadblocks

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 09:00 PM
To: Dan Wichman
Subject: RE: News

Never a dull moment!

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 6:29 PM
To: Martin Shkreli
Subject: Re: News

By the way I always appreciate your passion - I know you're in this for the right reasons (helping patients AND value creation), even if twitter is a scary place especially for an unfiltered ceo...anyway, hope NVS is on track and I'll harass barclays about that one.

Talk soon.

Dan

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 04:27 PM
To: Dan Wichman
Subject: RE: News

I don't think it matters. It's one drug out of 10 and doesn't generate revenue. It's important but what one guy says on twitter isn't going to change our fate. If anyone thinks the FDA is sitting there caring what I'm saying, they should sell our stock and move on.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:26 PM
To: Martin Shkreli
Subject: RE: News

It doesn't seem like a simple straightforward issue, but I hear you – it does seem like red tape could be too high in areas where there is no approved drug and the alternative is unavoidable death. We don't want families to have too much hope on something that may not work at all, but obviously the bar should not be super-high in situations such as these. I had thought you guys had respected the FDA's response and were going to address the issues quickly (and I assume you still are), but guess your views on it changed in the last few weeks.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:21 PM
To: Dan Wichman
Subject: RE: News

Sure FDA might say something like that, but it wouldn't be true and telling a family what they can or can't do to save their dying kid is crazy. The CEO of RARE believes the same thing, he is basically on a crusade against FDA on this very topic.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:17 PM
To: Martin Shkreli
Subject: RE: News

Ok, that sounds good, but don't you think FDA would also say, Retrophin didn't do a great job with the IND for xx and xx reasons, and sponsors owe it to the patients to do pristine jobs with filings such as this? Especially when you're putting a new drug into humans for the first time ever? Or am I crazy. Anyway, the tweeting I'm sure doesn't change much either way, I don't mind cringing now and then as long as you're doing all the right stuff behind the scenes and my confidence is high you're gonna create tons of value, which it is.

Though I must admit beyond the FDA thing, not sure why you need to ever respond to these idiotic retail guys who criticize you – who cares!

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:12 PM
To: Dan Wichman
Subject: RE: News

Sure, mobilizing people to get things to change. We think we could get the decision reversed. The FDA needs new compassionate use laws. Dying kids, etc. It's terrible. AIDS activists didn't let it go quietly into the night and companies were too embarrassed to say anything. The FDA isn't a judgmental crazy place, they use facts and come to decisions reasonably well. The idea they have orphan in the GI division is laughable and sad for people who have diseases like PKAN. We'll see if the activism works but I'm told >1,000 people have written the FDA and 7 senators have called them.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 4:08 PM
To: Martin Shkreli
Subject: RE: News

But is there anything to be gained? I know you're not into politics and diplomacy but not sure how it can possibly help you guys.
Not a big issue, but was pointed out to me by another investor who was turned off by it – I don't think it matters a huge amount but I did cringe reading those comments.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, May 05, 2014 4:05 PM
To: Dan Wichman
Subject: RE: News

don't think it makes a difference. The place turns over so fast and I have great relationships with lots of the key people.

From: Dan Wichman [redacted]
Sent: Monday, May 05, 2014 3:11 PM
To: Martin Shkreli
Subject: RE: News

Hey, hope weekend was good. Hadn't seen it but was brought to my attention by another investor – do you think it's a good idea to bash FDA on twitter? Seems like there isn't much to gain there unless you have some motive I don't know about. Am I crazy?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 8:48 AM
To: Dan Wichman
Subject: RE: News

So many legacy assets that people have just forgotten about. This is one of them. It is really a great drug that people need. Docs want more support, awareness, education. It's like Wilson's disease – there hasn't been a Wilson's presentation or symposium in decades thanks to Valeant/Aton/Merck. Docs hate that. Most of them don't know pricing, they just know support—how many reps they see, copays, etc.

The drug companies are afraid. Small ones, big ones, etc. Big price increases are horrifying because most executives overestimate changes in demand. It comes mostly from pharma's history as quasi-consumer products. The next generation of pharma guys (or the smart ones) understand the inelasticity of certain products. The insurers really don't care. They just pass it through and focus on managing care for physician payments and blockbusters. They assume someone will genericize it if it is making too much money, and they're right.

So I don't really think of it the same way as others. I think this deal, if we pull it off, is worth $100m-$200m to our company. We'll see!

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:41 AM
To: Martin Shkreli
Subject: Re: News

Interesting - sounds like a no-lose, to put it mildly. Don't have to run a model on that one this weekend to give you my opinion.

Funny that these small companies still haven't realized you can raise price aggressively and nobody gets too upset? Obviously depends on the product - but I figure this dynamic may not last forever, you need to maximize opportunities while you can. In the real boring spec pharma space I kind of look at hznp vs depo - own and like both companies, have nothing but good things to say about depo - but depo is very cautious and conservative, while hznp says, this price dynamic may not last forever at least on these reformulated pain products, so let's maximize our cash flows now and diversify over time. It's not like people are giving companies gold stars for charging slightly lower prices ("thanks guys for charging 500 an rx not 800") - in that land the generics aren't your competition and don't even try. Sorry that was a quick digression.

Anyway, it's different in orphan land, and probably more sustainable, but seems like at this point these little guys would get the idea that they could push things a bit. How can they ever make money with that model? Bottom line is I won't get too excited but it sounds very intriguing.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:23 AM
To: Dan Wichman
Subject: RE: News

The deal we're working on very simple and Manchester like.
We'd pay $1m to acquire a drug called Thiola, which is the only treatment for a rare disease called cystinuria (contrast with RPTP cystinosis – totally different).
The drug does $1.2m in sales. It is woefully underpriced and would not stop selling at orphan prices. With new pricing we estimate sales of $20 to $40 million. Almost 95% EBITDA margins at those prices. Would be an annuity for some time.

A $100m present for you this morning.
All kidding aside, it is still a medium stage negotiation and may not come to fruition. We have a good relationship with the seller and they have a contract sales force which we would use to sell the product, which would add $5m in expenses annually (for them that's another $1m or $2m margin) and a royalty. So it's something of a win-win but a capital W for us and a lowercase for them. It might finish in time to announce Novartis and this one.

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:19 AM
To: Martin Shkreli
Subject: Re: News

I'd say, I'll be happy with the one I know about, but I'm always open to more as long as you guys have the personnel and time and expertise to handle it all.
Glad Steve is on board - seems he knows you well at this point, and you haven't scared him away...
After the Wilson's frustration (which hopefully didn't scar him for life) seems you guys have come a long way.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:14 AM
To: Dan Wichman
Subject: RE: News

Yes, Steve is the best. We really trust and respect each other a huge amount – which is crucial to co-leading a company.

What if I told you we might announce two deals at once?

Hehehehe ☺

From: Dan Wichman [redacted]
Sent: Saturday, May 03, 2014 8:13 AM
To: Martin Shkreli
Subject: Re: News

Yes fair enough - once this deal closes I'll go back to being less of a pain in the a$$. Sounds good on Steve (a yin and yang perhaps?) and hope the other stuff works out.

Assuming this looks like a done deal this week (knock on wood), I'd love to discuss a little of how you'll convey it to the Street - I'm sure you've spent many hours thinking about that. Will be a fun opportunity. Hopefully your other investors agree the bigger deal is the better deal - but if not they're wrong!

Then I'll go back to leaving you alone and not harassing you semi-hourly - let you do the hard work in creating value.

Dan

Dan Wichman
Partner

[redacted]

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 07:57 AM
To: Dan Wichman
Subject: RE: News

I have to be careful with giving you minute by minute updates on the company ☺

Steve Aselage is joining as President and Chief Operations Officer – you've met him – he's on our Board and as former Chief Business Officer (similar role) at BioMarin I think he will help us not just in commercializing our drugs but also all aspects of the company – he is very savvy politically (has a very different approach from me), well-liked and will just make our company run a lot better across the board.

On Alvin, stay tuned.

From: Dan Wichman [redacted]
Sent: Friday, May 02, 2014 5:41 PM
To: Martin Shkreli
Subject: Re: News

Talked to Barclays - sounds like it's still on track. Fingers crossed for no new roadblocks I'm excited.
Any word on the r+d guy yet?

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 02:57 PM
To: Dan Wichman
Subject: RE: News

Yes. It should be a done deal. Never say never though.

From: Dan Wichman [redacted]
Sent: Thursday, May 01, 2014 2:45 PM
To: Martin Shkreli
Subject: RE: News

They've agreed to this? All parties? If so, that is great news, and we'd be very excited. Happy to pick up $10mln in pre-paid royalties to make those clowns happy. The npv is a no-brainer.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 2:41 PM
To: Dan Wichman
Subject: News

We are doing the entire deal at $190m. You twisted my arm!

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From: Dan Wichman [redacted]
Sent: Tuesday, May 27, 2014 2:17 PM
To: Martin Shkreli
Subject: RE: We are over the wall

Hey Martin – hope weekend was good. I didn't take a meeting with you guys because I don't think we need one – pretty straightforward and we'll definitely be involved here. But don't know if you have 5 minutes maybe to catch up later – not urgent. Thanks as always.

Dan

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Sunday, May 25, 2014 2:14 PM
To: Dan Wichman
Subject: RE: We are over the wall

Very reasonable, great people.

From: Dan Wichman [redacted]
Sent: Sunday, May 25, 2014 2:00 PM
To: Martin Shkreli
Subject: Re: We are over the wall

Ok fair enough, they're reasonable folks? I've definitely come across them before. Been around a long time.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Sunday, May 25, 2014 11:50 AM
To: Dan Wichman
Cc: Jim Tumbrink; Courtney Bond <courtney@retrophin.com>

Subject: RE: We are over the wall

I think they just want to sign this and we can discuss expansions shortly.

From: Dan Wichman [redacted]
Sent: Sunday, May 25, 2014 10:30 AM
To: Martin Shkreli
Cc: Jim Tumbrink; Courtney Bond
Subject: Re: We are over the wall

Thanks Martin, and nice to meet you Courtney. Seems like a no-lose deal. Are higher-dose formulations part of this deal? Clearly seems like a pretty straightforward way of moving the franchise forward. And why wouldn't all parties want to include an ER in this deal to get moving on it asap both from development and IP standpoint? Would think you and they would want to get moving right away for when this hits others' rather soon. Economic profile seems great. Anyway, seems like a matter of either very good npv, or ridiculous npv based on how the lifecycles play out.

Dan Wichman
Partner

[redacted]

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 24, 2014 10:06 PM
To: Dan Wichman
Cc: Jim Tumbrink; Courtney Bond <courtney@retrophin.com>
Subject: RE: We are over the wall

Hi Guys,

I am also CCing Courtney Bond who found the opportunity. Despite being 26, Courtney is starting to figure somewhat prominently in senior management. He is still very green, but he has come up with an inordinate number of good ideas. We're lucky to have him.

On GMs, it is strange, we buy the 100-pill packs for $50 each from Mission. So your average patient is going to be between $100-$150 per month in cost to us, or $1200-$1800 in COGS per year. This doesn't include the 20% royalty, obviously. So, if our price is $50k, the COSGS would be at most 4%. If the price is $100k, it is 1.8%.

Expenses are a good situation. Our MSL team is perfectly suited to educate on this product. Being a renal disease as well as a autosomal recessive genetic disease, we know this kind of stuff cold and leverages quite well. We will be hiring 10 sales people through Mission's contract sales force business. That should be about $2m.

ER is complicated because we have to sign a NEW deal with mission for both this and international. We don't think that will be hard but they will want another upfront, we think.

I agree it is irrationally low. Courtney is going to make a lot of money.

I agree it is very hard to find small volume products that go generic. Small revenue products go generic a lot – good example is Amphastar's cosyntropin (ACTH). But nothing small volume.

Courtney – Dan and Jim are two of our largest investors. They are big players in the specialty pharma business. Good guys to know.

Martin

From: Dan Wichman [redacted]
Sent: Friday, May 23, 2014 4:26 PM
To: Martin Shkreli
Cc: Jim Tumbrink
Subject: We are over the wall

Couple questions we have on your deal – we can speak about them live as well:
What are product GM's? assume 95%ish?
What expenses will you put on it? Assume small?
ER version development will start right away? This seems like a potentially compelling lifecycle strategy.
Why aren't they asking more from you guys? Understand it'll be a win-win, they're not the guys to make this big, but still seems almost irrationally low.
We couldn't think of small orphan products like this that have gone generic, but that may be based on the fact that they'd be so small we probably wouldn't have heard of them? We are trying to brainstorm.

Anyway, nothing not to like about this – it's just a matter of how good.

Talk to you soon.

Dan

Dan Wichman
Partner

[redacted]

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From: Dan Wichman [redacted]
Sent: Tuesday, September 23, 2014 12:38 AM
To: Martin@retrophin.com
Subject: Re: Hey

Excellent answer - thanks Martin. Appreciate the thoughtful response. I have no feel for how much momentum this may have - seems like any legislation is a long-shot for the foreseeable future in this Congress. And can't imagine this is high on the priority list. Not losing any sleep over it - but I was just curious. Generics don't do well with zero-volume drugs - just doesn't suit their model. And clearly the patient-centric approach does not fit generics well either. That said it's nice to have drugs that do have room for long-term improvement in the clinical profiles - in particular Thiola seems to have worlds of potential there.

Appreciate the thoughts - ain't us selling right now. I am very focused on the long-term (though like any fund I do get annoyed by short-term stupidity). Volume has been pretty decent. It will certainly be interesting to see the Q3 filings.

Dan Wichman
Partner

[redacted]

----- Original Message -----
From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, September 22, 2014 08:31 PM
To: Dan Wichman
Subject: RE: Hey

It should take a long amount of time because the Sherman act clearly states companies like Retrophin and Celgene have "no duty to deal" and the Supreme Court ratified two challenges to this in the Pac Bell and Verizon cases. So if they can get some legislative momentum and get a law signed, there will still be a 'test case' which has to prove this law supersedes the Sherman Act, which you may know is one of the oldest American pieces of legislation. So I think worst case we have another 5 years because once we hand over samples to a generic, they will have to spend the next 3 years getting an ANDA approved.

Thankfully we are not selling Tracleer or Revlimid -- these drugs are so small and we do not report to IMS, so I think we will stay under the radar.

Regarding my personal investments, I cannot comment too much other than my hope is to own as much of the company as possible and I would be patient as I reengineer to put myself in a position to do so. I have a very long-term mindset. I know we have a new hedge fund shareholder who just bought 1m+ shares, so it will be interesting to know who has sold (or is selling).

MS

-----Original Message-----
From: Dan Wichman [redacted]
Sent: Monday, September 22, 2014 8:28 PM
To: Martin Shkreli
Subject: Hey

Unrelated to my previous email (but still wondering on that) - curious any thoughts on the below? Seems it could make closed distribution trickier, but I have no idea where it is going...and I have always thought true long-term barriers to entry for you guys on Chenodal/Thiola will be new formulations:
http://blogs.wsj.com/pharmalot/2014/09/19/legislation-would-prevent-drug-makers-from-thwarting-generic-rivals/

Dan Wichman
Partner

[redacted]

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From: Martin Shkreli <Martin@retrophin.com>
Sent: Monday, June 02, 2014 2:02 AM
To: Jim Self
Subject: RE: Receipt of Agreement

I'm not much of a golfer unfortunately. So if you want to struggle through playing with us maybe that'd be okay, but it would be painful!
In the meantime we should grab dinner to celebrate the closing. When is good for you?

From: Jim Self [mailto:jim.self@missionpharmacal.com]
Sent: Friday, May 30, 2014 8:18 AM
To: Martin Shkreli
Subject: Re: Receipt of Agreement

Martin – trust me, no worries on this end. Just covering the bases if anyone had an issue. We are all good.

I think I need to come to New York. Or if you are a golfer, you can come here and we can play 18 and spend some time on our priorities and other opportunities for us to work together. At Mission we have a BD team of 1, so I happy to work with others.

Let me know what times may work for me to visit with you guys, or if you are interested in golf, we can get that on the books as well.

This was seriously the fastest I've ever seen these types of deals get done. Nice job of removing the minutia and keeping the rails greased. Thank you!

Respectfully,

Jim Self
Vice President, Corporate Business Development
Mission Pharmacal
111 East Court Street, Doylestown, PA 18901-3743

Cell: 215-588-9311 | Email: jim.self@missionpharmacal.com

Corporate Office: 10999 Interstate Highway 10 West, Suite 1000, San Antonio, TX 78230

From: Martin Shkreli <Martin@retrophin.com>
Date: Friday, May 30, 2014 at 7:53 AM
To: Jim Self <jim.self@missionpharmacal.com>
Subject: RE: Receipt of Agreement

Thanks for your patience and understanding on this. Monday is the Jefferies conference – so we ordinarily would never front-run something like this, but we simply couldn't put this news out on Monday according to our biggest shareholder (their wish is my command). With the $80,000,000 Barclays financing, I trust you know we are good for it! We will be sending the funds today.

In other news, what are Mission's priorities? My 17-person BD team is at your disposal to help you seek out the assets you need to grow your company on attractive terms. Anything at all I can do to help, I will break my butt to do so. I know almost every drug CEO on the planet.

Martin

From: Jim Self [mailto:jim.self@missionpharmacal.com]
Sent: Thursday, May 29, 2014 2:49 PM
To: Martin Shkreli
Subject: Re: Receipt of Agreement

Ideally I know our CFO would like them today if possible. If tomorrow is the soonest they can be sent, I can provide cover.

On the press release, I just sent Courtney and Ron the edited release which includes the fair balance info required by the FDA. Also, I just need to coordinate the internal communication to others in Mission, but more importantly the salesforce that may receive questions from their doctors.

Respectfully,

Jim Self
Vice President, Corporate Business Development
Mission Pharmacal
111 East Court Street, Doylestown, PA 18901-3743

Cell: 215-588-9311 | Email: jim.self@missionpharmacal.com

Corporate Office: 10999 Interstate Highway 10 West, Suite 1000, San Antonio, TX 78230

From: Martin Shkreli <Martin@retrophin.com>
Date: Thursday, May 29, 2014 at 2:16 PM
To: Jim Self <jim.self@missionpharmacal.com>
Subject: RE: Receipt of Agreement

Thanks Jim – the sooner the better on the press release. We have raised $80,000,000 and this whole thing is pretty crazy. Can we send you the funds tomorrow? We want to put out press releases tonight. The release clearly says 'financial terms are not disclosed'. The reason for doing it tonight is the Jefferies conference is Monday and we want to make sure people see the news.

From: Jim Self [mailto:jim.self@missionpharmacal.com]
Sent: Thursday, May 29, 2014 1:48 PM
To: Martin Shkreli
Subject: Re: Receipt of Agreement

Wow...you and I need to meet.

We have some edits to the Press Release, just to be consistent with required FDA ISI information. I'll send that along shortly.

I do look forward to meeting...

Respectfully,

Jim Self
Vice President, Corporate Business Development
Mission Pharmacal
111 East Court Street, Doylestown, PA 18901-3743

Cell: 215-588-9311 | Email: jim.self@missionpharmacal.com

Corporate Office: 10999 Interstate Highway 10 West, Suite 1000, San Antonio, TX 78230

From: Martin Shkreli <Martin@retrophin.com>
Date: Thursday, May 29, 2014 at 1:42 PM
To: Jim Self <jim.self@missionpharmacal.com>
Subject: RE: Receipt of Agreement

Great! Consistent with that, we were able to raise $85,000,000 through Barclays to fund this acquisition and some future activities. We are thrilled. I will send you that final press release as well as the Thiola one.

From: Jim Self [mailto:jim.self@missionpharmacal.com]
Sent: Thursday, May 29, 2014 1:34 PM
To: Martin Shkreli
Subject: Re: Receipt of Agreement

Yes all is well. I am awaiting signature from Texas...Will send final copies and wire instructions in just a bit...

Respectfully,

Jim Self
Vice President, Corporate Business Development
Mission Pharmacal
111 East Court Street, Doylestown, PA 18901-3743

Cell: 215-588-9311 | Email: jim.self@missionpharmacal.com

Corporate Office: 10999 Interstate Highway 10 West, Suite 1000, San Antonio, TX 78230

From: Martin Shkreli <Martin@retrophin.com>
Date: Thursday, May 29, 2014 at 1:32 PM
To: Jim Self <jim.self@missionpharmacal.com>
Subject: Receipt of Agreement

Hi Jim,

I just wanted to make sure you received our signed agreement.

Best,
Martin

Retrophin

Investor Presentation
May 2014

Retrophin

Forward-Looking Statements

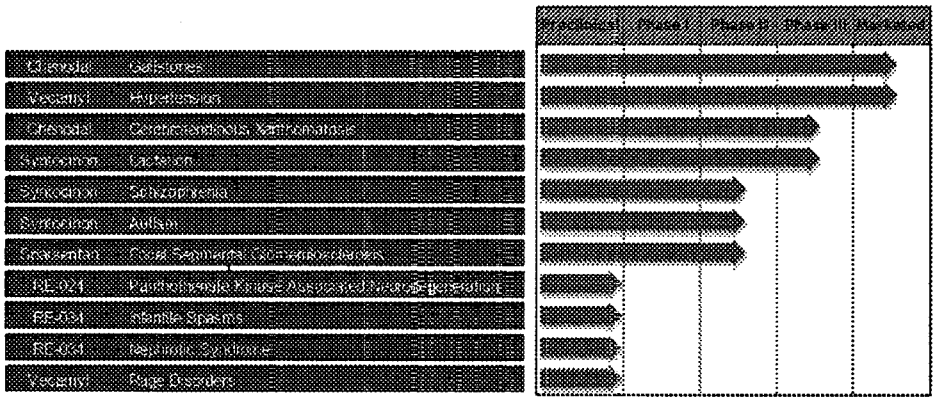
This presentation contains forward-looking statements, including statements about our prospects, competitive position, regulatory filings and agency actions, and the anticipated development, timing, data readouts and therapeutic scope of programs in our clinical pipeline. These forward-looking statements may be accompanied by such words as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "project," "target," "will" and other words and terms of similar meaning. You should not place undue reliance on these statements.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including the safety and efficacy of our product candidates, product competition, the occurrence of adverse safety events with our products, adverse market and economic conditions, our dependence on collaborations and other third parties over which we may not always have full control, failure to comply with government regulation, our ability to protect our intellectual property rights, and have sufficient rights to market our products and services together with the cost of doing so, problems with our manufacturing processes and our reliance on third parties, our ability to attract and retain qualified personnel, our level of indebtedness, environmental risks, change of control provisions in our collaborations and the other risks and uncertainties that are described in the Risk Factors section of our most recent annual or quarterly report and in other reports we have filed with the SEC.

These statements are based on our current beliefs and expectations and speak only as of the date of this presentation. We does not undertake any obligation to publicly update any forward-looking statements.

2

Pipeline



1. We intend to file an application with the FDA for marketing approval in 2014
2. We are partially funding a clinical trial studying the effects of oxytocin in the treatment of schizophrenia, which is being conducted by the University of California, San Diego

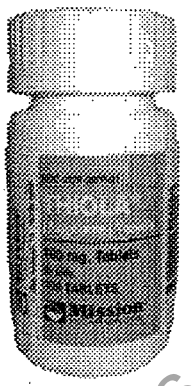
3

Transaction Overview

- Retrophin has signed a term sheet to license Thiola from Mission Pharmacal based in San Antonio, TX
  - $3mm upfront payment
  - Ongoing 20% royalty on sales
  - Represents 2x multiple on current sales
  - Highly accretive transaction for Retrophin
- Retrophin has identified several potential strategies to grow both volumes and pricing
  - Retrophin believes Thiola is significantly underpriced relative to the benefit it offers
  - Current focus appears low and the product is not actively promoted
  - Retrophin plans to move Thiola to specialty distribution
  - Opportunity to expand approved territories
- Strong fit with Retrophin's focus on rare and catastrophic diseases

Thiola (Tiopronin)

- Thiola is an FDA approved small molecule for the prevention of cystine formation
  - Approved in 1988
  - Granted Orphan Drug Designation
  - No known generics on file at this time
- Thiola is one of two products approved to prevent stone formation in cystinurics
  - Thiola PPPY ~$4,000-8,000
  - Competitor product PPPY ~$80,000-140,000
- Thiola is the preferred therapy due to its reduced risk of adverse events



Gross Sales ($mm)

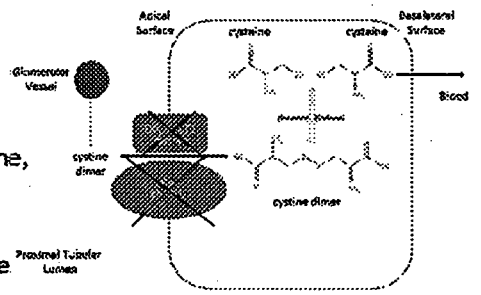
2009	2010	2011	2012	2013
1.39	1.66	1.86	1.94	1.83

Source: Mission Pharmacal

5

Cystinuria

- Cystinuria is a rare genetic disease
- Autosomal recessive inheritance
- Mutations in SLC3A1 and SLC7A9
- Trans-epithelial transporters of cystine, ornithine, lysine, and arginine
- Cystine is a dimer composed of two cysteine residues bound by a disulfide bond
- Cystine is not readily soluble
- Cystine accumulation leads to the formation of cystine stones
- Kidney stones are typically removed via lithotripsy or nephrolithotomy
- Chronic kidney stones can cause long term renal damage



Epidemiology

- The incidence of cystinuria is 1 : 7,000 worldwide
- There are believed to be 10,000 cystine stone formers in the US
  - Some of these patients can have their cystinuria controlled with diet, increased fluid intake, and alkalization therapy
  - Some cystinurics are still unable to manage their disease using these methods
- Thiola helps these patients control the formation of stones
- If left untreated cystinurics can have up to 5 stone events per year
- Cost of a single stone removal
  - Lithotripsy: $10,000-$20,000
  - Nephrolithotomy: $20,000-$60,000

7

Intellectual Property

- Similar to Chenodal, Retrophin will place Thiola into closed distribution
  - Closed distribution system prevents generics from accessing the product for bioequivalence studies
- Retrophin will also increase the number of available dosage forms
  - 100mg capsule is currently the only available dose
  - Retrophin will develop 250mg and 500mg doses
- Retrophin also plans to develop a long-acting version of Thiola for once daily dosing

8

Cystinuria Dedicated Sales Force

Retrophin

Alamo PHARMA SERVICES

Coverage

- 10 contract sales reps

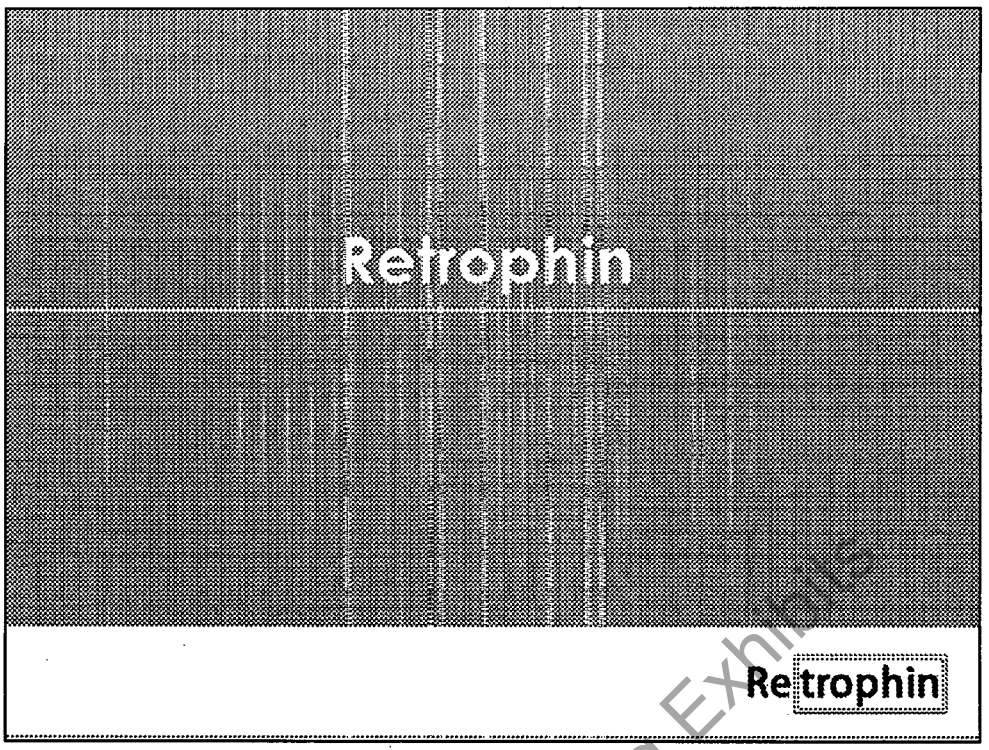
Rep Profile

- Retrophin nephrology/urology sales force will be staffed by trained Alamo sales reps
- Alamo employees

Timing

- 3-4 months for full deployment

9



From: Redacted
Sent: Saturday, May 03, 2014 1:04 PM
To: Martin@retrophin.com
Subject: Re: News

Funny how suddenly in the same week MRK, SNY, ABT are all rumored to sell legacy product portfolios. Fascinating times. All this m+a, asset swapping, divestitures and such should provide years of opportunities for you guys and many others.

I hear you on the pharma mentality - it's ironic how it took two companies - jazz and hznp - the brink of insolvency to decide they should aggressively play the price card. Very different dynamics but basically each company would likely have gone under without those moves, but it took extreme weakness to force that hand. And qcor is obviously a poster-child - for the heat and bad PR they took, didn't work out so badly in the end, did it? Not every deal and every product will work out like these, but for smart managements, that are resourceful and opportunistic, these are exciting times.

Redacted
Partner

Redacted

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:47 AM
To: Redacted
Subject: RE: News

So many legacy assets that people have just forgotten about. This is one of them. It is really a great drug that people need. Docs want more support, awareness, education. It's like Wilson's disease – there hasn't been a Wilson's presentation or symposium in decades thanks to Valeant/Aton/Merck. Docs hate that. Most of them don't know pricing, they just know support—how many reps they see, copays, etc.

The drug companies are afraid. Small ones, big ones, etc. Big price increases are horrifying because most executives overestimate changes in demand. It comes mostly from pharma's history as quasi-consumer products. The next generation of pharma guys (or the smart ones) understand the inelasticity of certain products. The insurers really don't care. They just pass it through and focus on managing care for physician payments and blockbusters. They assume someone will genericize it if it is making too much money, and they're right.

So I don't really think of it the same way as others. I think this deal, if we pull it off, is worth $100m-$200m to our company. We'll see!

From: Redacted
Sent: Saturday, May 03, 2014 8:41 AM
To: Martin Shkreli
Subject: Re: News

Interesting - sounds like a no-lose, to put it mildly. Don't have to run a model on that one this weekend to give you my opinion.

Funny that these small companies still haven't realized you can raise price aggressively and nobody gets too upset? Obviously depends on the product - but I figure this dynamic may not last forever, you need to maximize opportunities while you can. In the real boring spec pharma space I kind of look at hznp vs depo - own and like both companies, have nothing but good things to say about depo - but depo is very cautious and conservative, while hznp says, this price dynamic may not last forever at least on these reformulated pain products, so let's maximize our cash flows now and diversify over time. It's not like people are giving companies gold stars for charging slightly lower prices ("thanks guys for charging 500 an rx not 800") - in that land the generics aren't your competition and don't even try. Sorry that was a quick digression.

Anyway, it's different in orphan land, and probably more sustainable, but seems like at this point these little guys would get the idea that they could push things a bit. How can they ever make money with that model? Bottom line is I won't get too excited but it sounds very intriguing.

Redacted
Partner

Redacted

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:23 AM
To: Redacted
Subject: RE: News

The deal we're working on very simple and Manchester like.
We'd pay $1m to acquire a drug called Thiola, which is the only treatment for a rare disease called cystinuria (contrast with RPTP cystinosis – totally different).
The drug does $1.2m in sales. It is woefully underpriced and would not stop selling at orphan prices. With new pricing we estimate sales of $20 to $40 million. Almost 95% EBITDA margins at those prices. Would be an annuity for some time.

A $100m present for you this morning.
All kidding aside, it is still a medium stage negotiation and may not come to fruition. We have a good relationship with the seller and they have a contract sales force which we would use to sell the product, which would add $5m in expenses annually (for them that's another $1m or $2m margin) and a royalty. So it's something of a win-win but a capital W for us and a lowercase for them. It might finish in time to announce Novartis and this one.

From: Redacted
Sent: Saturday, May 03, 2014 8:19 AM
To: Martin Shkreli
Subject: Re: News

I'd say, I'll be happy with the one I know about, but I'm always open to more as long as you guys have the personnel and time and expertise to handle it all.
Glad Steve is on board - seems he knows you well at this point, and you haven't scared him away...

After the Wilson's frustration (which hopefully didn't scar him for life) seems you guys have come a long way.

Redacted
Partner

Redacted

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 08:14 AM
To: Redacted
Subject: RE: News

Yes, Steve is the best. We really trust and respect each other a huge amount – which is crucial to co-leading a company.

What if I told you we might announce two deals at once?

Hehehehe ☺

From: Redacted
Sent: Saturday, May 03, 2014 8:13 AM
To: Martin Shkreli
Subject: Re: News

Yes fair enough - once this deal closes I'll go back to being less of a pain in the a$$. Sounds good on Steve (a yin and yang perhaps?) and hope the other stuff works out.

Assuming this looks like a done deal this week (knock on wood), I'd love to discuss a little of how you'll convey it to the Street - I'm sure you've spent many hours thinking about that. Will be a fun opportunity. Hopefully your other investors agree the bigger deal is the better deal - but if not they're wrong!

Then I'll go back to leaving you alone and not harassing you semi-hourly - let you do the hard work in creating value.

Redacted

Redacted
Partner

Redacted

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Saturday, May 03, 2014 07:57 AM

To: Redacted
Subject: RE: News

I have to be careful with giving you minute by minute updates on the company ☺

Steve Aselage is joining as President and Chief Operations Officer – you've met him – he's on our Board and as former Chief Business Officer (similar role) at BioMarin I think he will help us not just in commercializing our drugs but also all aspects of the company – he is very savvy politically (has a very different approach from me), well-liked and will just make our company run a lot better across the board.

On Alvin, stay tuned.

From: Redacted
Sent: Friday, May 02, 2014 5:41 PM
To: Martin Shkreli
Subject: Re: News

Talked to Barclays - sounds like it's still on track. Fingers crossed for no new roadblocks I'm excited.
Any word on the r+d guy yet?

Redacted
Partner

Redacted

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 02:57 PM
To: Redacted
Subject: RE: News

Yes. It should be a done deal. Never say never though.

From: Redacted
Sent: Thursday, May 01, 2014 2:45 PM
To: Martin Shkreli
Subject: RE: News

They've agreed to this? All parties? If so, that is great news, and we'd be very excited. Happy to pick up $10mln in pre-paid royalties to make those clowns happy. The npv is a no-brainer.

Redacted
Partner

Redacted

212-808-2462 – work
212-808-2464 – fax

From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Thursday, May 01, 2014 2:41 PM
To: Redacted
Subject: News

We are doing the entire deal at $190m. You twisted my arm!

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From: Courtney Bond [redacted]
Sent: Thursday, May 22, 2014 11:10 PM
To: nikhil.[redacted]@barclays.com
Subject: RE: Question on competitor

Sure. 646 564 3679

From: nikhil[redacted]@barclays.com [redacted]
Sent: Thursday, May 22, 2014 7:09 PM
To: Courtney Bond
Subject: RE: Question on competitor

Thanks Courtney. Can I give you a quick call to ask couple of clarifying questions?

From: Courtney Bond[redacted]
Sent: Thursday, May 22, 2014 7:06 PM
To: Goel, Nikhil: IBD (NYK);[redacted], Edwin Urrutia
Cc: Burkly, Thomas: IBD (NYK); Caracciola, Derek: IBD (NYK); Curtis, Daniel: IBD (NYK); Bates, Jessica: IBD (NYK)
Subject: RE: Question on competitor

1. There are currently 300-400 patients on Thiola right now. There likely aren't any patients on Thiola for Wilson's. There's no way to accurately estimate how many patients take penicillamine for cystinuria since Wilson's is the major indication.
2. See answer #1.
3. Physicians prefer Thiola over Cuprimine because the adverse event profile for Thiola is better. Cuprimine is a very harsh therapy and patients who are allergic to penicillin are also allergic to penicillamine. Thiola is also believed to be more efficacious but that is based on anecdotal evidence.
4. We talked to a handful of doctors who treat cystinuria and none have ever been approached by Mission or Valeant.

Hope this helps.

From: nikhil[redacted]@barclays.com [mailto:nikhil.goel@barclays.com]
Sent: Thursday, May 22, 2014 6:44 PM
To: 'courtney[redacted]; Edwin Urrutia
Cc: thomas.[redacted]@barclays.com; derek.caracciola@barclays.com; daniel.[redacted]@barclays.com; jessica.bates@barclays.com
Subject: Question on competitor

Courtney and Edwin,

One of the investor mentioned that Cuprimine is priced so high because it is indicated for Wilson's disease and price increase for Thiola can't be justified based on Cuprimine's high price. We answered by saying that we are not modeling any patients increase and because this drug is such a small spend for managed care companies, there won't be any push back from the managed care companies as we saw with Chenodal but it would be good to understand some of the questions below as other investors might raise it too:

1) How many patients take it? If possible to have a breakdown between cystinuria and Wilsons disease.
2) Split between the sales for "Wilson's disease" and "cystinuria"

3) Let's assume that the price is same for both Cuprimine and Thiola, would doctors prescribe Cuprimine over Thiola or Thiola over Cuprimine? Main intent of this question is if we increase the price of Thiola, do we run a risk of losing 400 patients we have currently on Thiola?
4) Does Valeant actively promote Cuprimine for cystinuria or Wilsons disease?

Thanks,
Nikhil

Nikhil Goel
BARCLAYS
Investment Banking Division | Global Healthcare
[redacted]
New York, NY 10019
[redacted]

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April 2, 2015
OUTPERFORM

Joseph P. Schwartz
[redacted]
Paul Matteis
[redacted]

LEERINK

Reason for report:
INITIATION

RETROPHIN, INC.

Initiating at OP; Commercial & Clinical Execution Oppty's to Drive Stock Higher

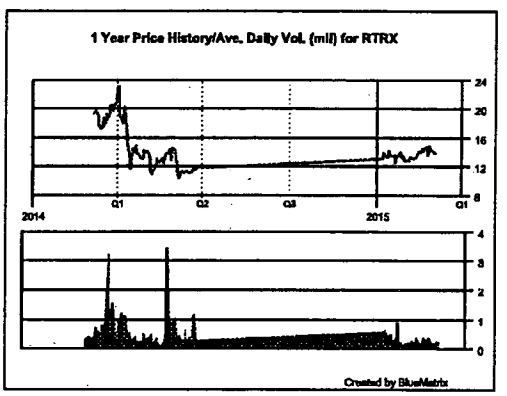
• **Bottom Line:** We are initiating coverage of RTRX shares with an Outperform rating and $48 price target in 12 months. We believe the company's investment-minded strategy of acquiring under-appreciated commercial- or late-stage therapies for rare "orphan" diseases is likely to generate attractive returns for shareholders now that the company is being led by a seasoned management team with significant operating experience. We believe that the next 12-18 months are poised to present multiple opportunities for RTRX to create shareholder value from both marketed products and the development pipeline.

• **MEDACorp specialist feedback has been positive on the attributes of the company's approved products** (Thiola for cystinurea, Chenodal for cerebrotendinuous xanthomatosis [CTX] and Cholbam for rare bile acid synthesis disorders); we expect the company to execute on established tactics to find patients who can benefit from therapy and help them obtain reimbursement at premium pricing. RTRX management is committed to doing so, while employing a capital-efficient business model that we believe can generate cash flow in a sustainable manner.

• **We also believe pipeline news flow can provide significant upside for the stock going forward.** We are encouraged by the development rationale for the company's pipeline programs (sparsentan for focal segmental glomerulosclerosis [FSGS], RE-024 for pantothenate kinase-associated neurodegeneration [PKAN], and RE-034 [synthetic adrenocorticotropic hormone/ACTH] for indication[s] to be determined that are already approved for use of porcine-derived Acthar Gel).

• **We believe the RTRX pipeline receives little, if any, credit at the current market valuation.** We estimate ~$950MM and $250MM gross market opportunities for sparsentan and RE-024 with 65% and 50% probabilities of launch in 2018 and 2019, respectively. RE-034 is not yet reflected in our model or valuation, pending further visibility into the lead indication and development pathway; however, based on the established precedent of Acthar Gel, we are intrigued by the potential to develop the company's synthetic ACTH in an overlapping area such as nephrotic syndrome or neurological disease. In addition, RTRX may continue to add complementary assets that leverage its development and commercial capabilities further. Lastly, we believe that RTRX may be able to monetize the pediatric review voucher (PRV) received with the recent Cholbam approval to improve its balance sheet further.

Key Stats:	(NASDAQ:RTRX)
S&P 600 Health Care Index:	1,637.91
Price:	$23.61
Price Target:	$48.00
Methodology:	DCF analysis
52 Week High:	$24.71
52 Week Low:	$7.85
Shares Outstanding (mil):	34.4
Market Capitalization (mil):	$812.2
Book Value/Share:	$5.08
Cash Per Share:	$4.40
Net Debt to Total Capital:	32%
Dividend (ann):	$0.00
Dividend Yield:	0.0%



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	PE
2014A	–	$6.0	$8.3	$14.1	$28.4	–	($2.46)	($0.73)	($1.10)	($4.29)	NM
2015E	$16.7	$20.9	$23.6	$26.9	$92.1	($0.51)	($0.39)	($0.32)	($0.26)	($0.97)	NM
2016E	–	–	–	–	$137.1	–	–	–	–	($0.04)	NM

Source: Company Information and Leerink Partners LLC Research
Revenues in millions. Results in 2Q14 are from 1H15 as they are not broken out by quarter.
EPS are GAAP. Quarterly EPS may not add to annual total due to change in shares outstanding.

LEERINK

RETROPHIN (NASDAQ: RTRX): Initiating at OP; Commercial and Clinical Execution Opportunities to Drive Stock Higher

JOSEPH P. SCHWARTZ
MANAGING DIRECTOR
BIOTECHNOLOGY ANALYST
[redacted]

Paul Matteis
ASSOCIATE
BIOTECHNOLOGY
[redacted]

INVESTMENT THESIS

We rate RTRX shares Outperform. We believe the company's investment-minded strategy of acquiring under-appreciated commercial- or late-stage therapies for rare "orphan" diseases is likely to generate attractive returns for shareholders now that the company is being led by a seasoned management team with significant operating experience. MEDACorp specialist feedback has been positive on the attributes of the company's approved products (Thiola for cystinurea, Chenodal for cerebrotendinuous xanthomatosis [CTX] and Cholbam for rare bile acid synthesis disorders); we expect the company to execute on established tactics to find patients that can benefit from therapy and help them obtain reimbursement at premium pricing. RTRX management is committed to doing so while employing a capital-efficient business model that we believe can generate cash flow in a sustainable manner. We also believe pipeline news flow can provide significant upside for the stock going forward. We are encouraged by the development rationale for the company's pipeline programs (sparsentan for focal segmental glomerulosclerosis [FSGS], RE-024 for pantothenate kinase-associated neurodegeneration ([KAN], and RE-034 [synthetic adrenocorticotropic hormone/ACTH] for indication[s] to be determined that are already approved for use of porcine-derived Acthar Gel). We estimate ~$950MM and $250MM gross market opportunities for sparsentan and RE-024 with 65% and 50% probabilities of launch in 2018 and 2019, respectively. RE-034 is not yet reflected in our model or valuation, pending further visibility into the lead indication and development pathway. In addition, RTRX may continue to add complementary assets that leverage its development and commercial capabilities further.

We Continue to Believe That Premium Pricing for Ultra-Orphan (and Most Orphan) Drugs Is Sustainable for the Foreseeable Future

LEERINK

Retrophin's practice of acquiring under-appreciated therapies and raising the price many-fold has raised eyebrows; however, doing so puts the company at the price level of its industry peers which allows it to continue to invest in resources for existing patients and identification of new patients who would otherwise fall through the cracks in the healthcare system, which is generally not designed to cater to patients with rare diseases.

Our latest MEDACorp survey of 30 payors with over 90MM lives in the US on orphan drug spending (LINK) placed just ~17%, ~28%, and ~35% probabilities that their coverage policies for orphan drugs will change by 2016, 2018 and 2020. We believe this contrasts with cautious investor expectations that the orphan drug business model is unsustainable and could come under increased payor regulation in the near term.

For those able to estimate, orphan drugs remain a small part of payors' budgets, comprising an estimated ~6% of pharmacy spend and ~5% of medical spend on average. Centers for Medicare and Medicaid Services estimates that prescription drugs are ~10% of U.S. healthcare spending, implying that orphan drugs are ~0.5% of the healthcare budget. Thus, we continue to believe that a distinction should be drawn between the sticker shock and budget impact of orphan drugs.

When deciding whether or not to reimburse for an orphan drug, of higher importance to payors than cost is whether or not a therapeutic alternative exists, which along with other commentary suggests to us that payors can only impose significant coverage/access restrictions when they can direct patients onto another agent. This bodes well for RTRX in our view, which markets products that are priced at a premium but are the only drugs approved for their respective conditions.

VALUATION: DCF Analysis Implies ~100% Upside from Current Levels

- We believe the current stock price can be justified by the growth opportunities for the base business, inclusive of Thiola, Chenodal, and Cholbam.
- Notably, we believe the RTRX pipeline receives little, if any, credit at the current market valuation.
  - We estimate ~$950MM and $250MM gross market opportunities for sparsentan and RE-024 with 65% and 50% probabilities of launch in 2018 and 2019, respectively.
  - RE-034 is not yet reflected in our model or valuation, pending further visibility into the lead indication and development pathway.
- Our DCF analysis indicates a ~$48 price target in 12 months.

Retrophin DCF Analysis	2014	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	TV
Cash Flow From Operations ($MM)	(45.89)	(34.72)	(1.57)	11.23	21.81	47.26	81.30	125.76	158.99	184.27	222.88	239.12	171.28	133.81	102.00	
Cash Flow From Investing ($MM)	(37.78)	(6.00)	(6.30)	(6.62)	(6.95)	(7.29)	(7.66)	(8.04)	(8.44)	(8.86)	(9.31)	(9.77)	(10.26)	(10.78)	(11.31)	
Net Borrowing (Repayment) ($MM)																
Free Cash Flow ($MM)	(83.67)	(40.72)	(7.87)	4.61	14.86	39.96	73.65	117.72	150.55	175.40	213.57	229.35	161.02	123.04	90.68	924.97
Discount Periods	-	-	0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75	
NPV FCF ($MM)	(83.7)	(40.7)	(7.9)	4.6	14.9	40.0	73.6	117.7	150.6	175.4	213.6	229.4	161.0	123.0	90.7	218.07

Sum NPV FCF ($MM)	1,480
Net Cash 1Q15	67
Pediatric PRV	96
Implied RTRX Mkt Cap ($MM)	1,645
RTRX Per Share Value	47.77

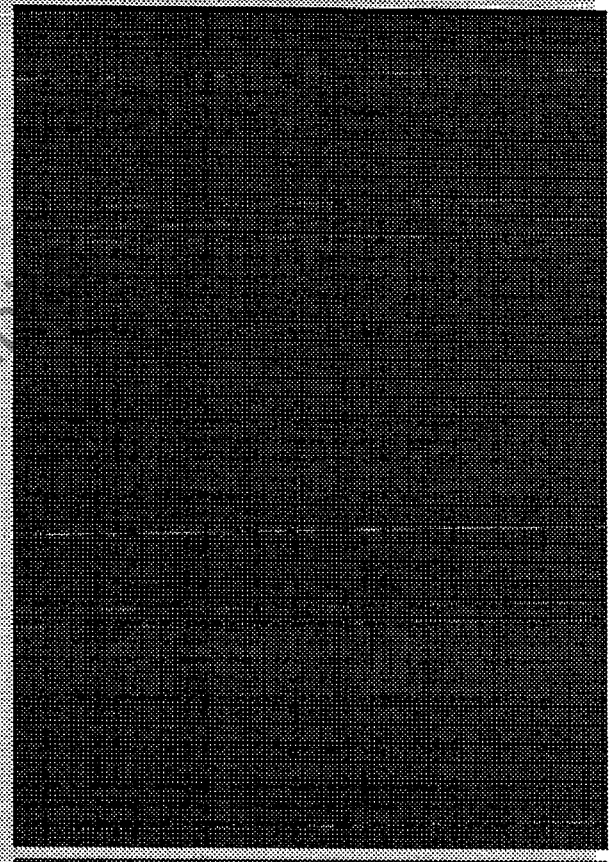
Cost of Equity	12%
Terminal Growth Rate	2%
Diluted Shares Outstanding	34.4

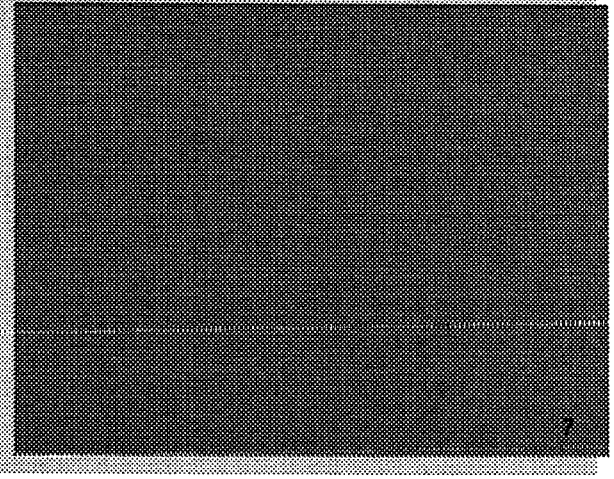
Source: Leerink Partners Research

RISKS TO VALUATION

Risks to Valuation include potential commercial, clinical and regulatory disappointments across the company's existing products, including Thiola, Cholbam and Chenodal and development pipeline, including Sparsentan and RE-024, all of which contribute in material ways to our valuation. In particular, commercial execution on Thiola and intangible value of Pediatric PRV are key to driving near-term revenues for the company that may help justify the existing liabilities on the balance sheet. Additional risks may exist to commercialization of Cholbam and Chenodal if the company is unable to identify patients in these ultra-orphan diseases.

Company Overview





RTRX Company Overview

- Fully integrated biopharmaceutical company focused on disease areas in which the industry has, to date, had limited interest or effectiveness
  - One core area is development of orphan drugs for the treatment of rare catastrophic diseases

- Backed by a seasoned management and scientific team that is uniquely positioned to
  - identify under-utilized assets
  - conduct in-house drug discovery to find the fastest path to approval for its drug in development

- Next 12-18 months present multiple opportunities for RTRX to generate shareholder value
  - two commercial products, in particular Thiola that is currently in acceleration mode following its re-launch in 3Q14
  - robust R&D pipeline driven by ph. II asset sparsentan in an underserved Focal Segmental Glomerulosclerosis (FSGS) disease, with the likely potential to file for accelerated approval by 2Q16
  - Additional pipeline value may be created as RE-024 and RE-034 enter the clinic

- Business development capabilities, including a team of 12 employees, are emphasized as a significant driver of shareholder value in terms of near-term revenue accretion and supplement portfolio with late-stage clinical or commercial rare disease assets

Source: Leerink Partners Research, Company Reports

LEERINK

Three Pillars of Sustained Growth, in Mgmt's View

Commercial Platform *(measure of execution)*

Thiola (tiopronin) tablets **for kidney stones in Cytinuria**

- Beating on 2014 goal for ~450 pts to resume treatment following supply shortage from original manufacturer post-acquisition in 2Q14
- Rate of new pts accompanied with increasing compliance & adherence
- Price increase of ~20X to $85K PPY

CHENODAL **for Cerebrotendinuous Xanthomatosis (CTX)**

- Low-single-digit growth in CTX pts with upside contingent upon ongoing efforts in patient identification
- Pursuit of an official label for CTX by YE15 through an ongoing collaborative dialogue with FDA
- Minimal pushback from payers on an orphan drug pricing in the range of $500K PPY

CHOLBAM **for Rare Bile Acid Disorders**

- On the heels of FDA approval in Mar'15, more clarity remains to come on both epidemeology (monogenic and peroxisomal) and pricing
- Pediatric Review Voucher granted with approval adds an unexpected ~$100MM to NPV

Pipeline Potential *(call options)*

Sparsentan In FSGS

- Last patient enrolled in registration-enabling Ph. 2 by YE15
- 8-week Proteinuria primary endpoint may lead to NDA filing by mid-2016
- Worth ~$25 in our PT; may present further upside of ~$15

RE-024 in PKAN

- US IND to be completed in 1H15
- Initiation of Ph. 1 study by YE15
- Worth ~$9 in our PT; may present further upside of ~$10

PE-034 in ACTH

- Possible US IND in 2015
- Not included in our valuation

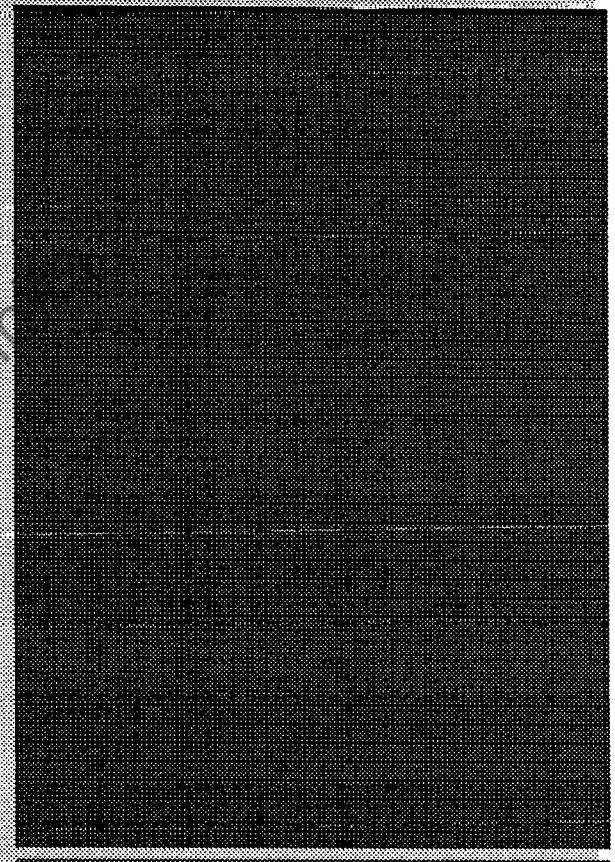
Business Development

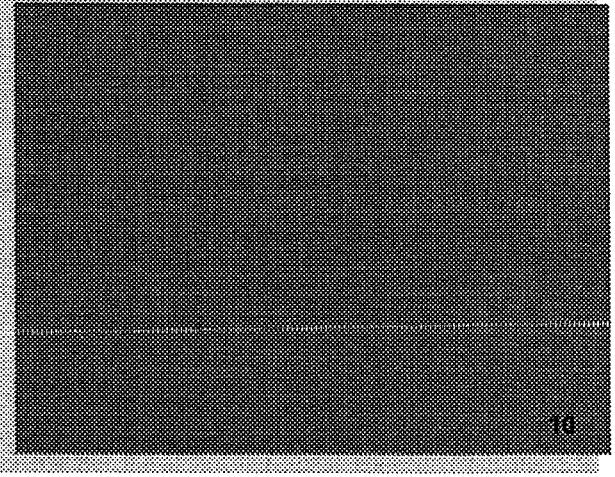
- ✓ **Near Term Accretive**
- ✓ **Rare-disease focus**
- ✓ **Minimal infrastructural needs**
- ✓ **Late-stage clinical or commercial stage**

Source: Leerink Partners Research, Company Reports

Thiola for Prevention of Cystine Kidney Stone Formation

Thiola®
(tiopronin) tablets
Rx Only



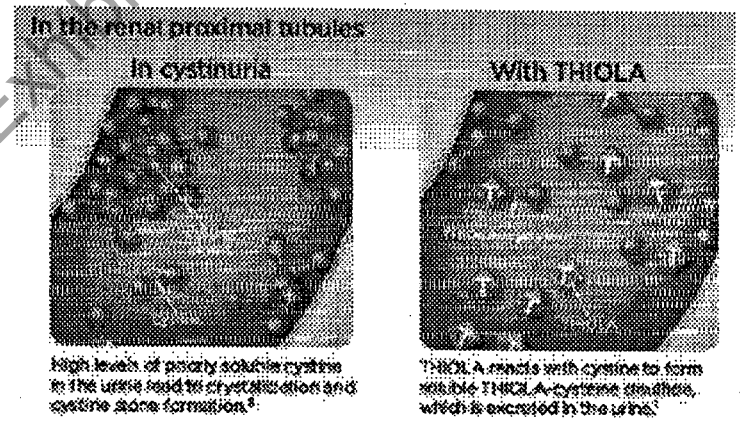


Current Revenue Streams Are Largely Driven by Thiola's Re-Launch in the Cystinuria Market

LEERINK

- Originally acquired from Mission Pharmacal Company (private) in 2Q14, Thiola (triopin) is the only FDA-approved small molecule for the prevention of cystine stone formation

- Thiola is administered prophylactically and works by binding with cystine to form a more soluble molecule that can be easily excreted in the urine
  - If left untreated, cystinuria patients can have multiple stone events/year, which do not respond to lithotripsy and require surgical intervention leading to increased morbidity, pain, and costs to the healthcare system



- In clinical studies, Thiola has been shown to significantly reduce the number of stone events in pts with cystinuria

	Naive to d-penicillamine (n=14)	Previously treated to d-penicillamine (n=43)
Stone reduction *(reduced rate of new formation)*	94.1%	81.4%
Stone remission *(cessation of stone formation)*	71.4%	62.8%

- MEDACorp specialists consider Thiola to be the only non-invasive pharmacological option they currently have to effectively manage their patients with cystinuria, with d-pencillamine often not preferred due to its severe side effect profile (liver tox., cytopenias, induced SLE, etc.)

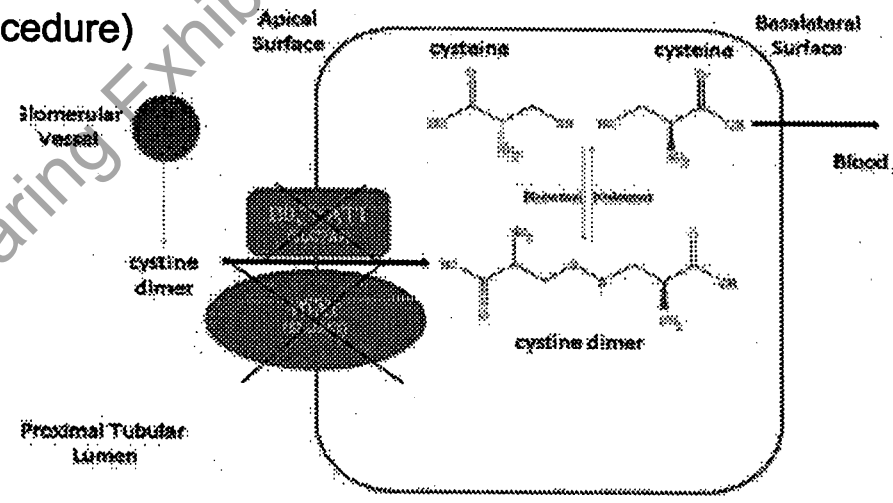
Source: Leerink Partners Research, Company Reports

Kidney Stones Due to Hereditary Cystinuria Represent a Significant Symptomatic Unmet Need

LEERINK

- Typically, kidney stones are removed via lithotripsy/nephrolithomy, which is a ~1 hour procedure of passing high-energy shock (sound) waves through the body until they hit kidney stones and break them into tiny pieces
  - Costs $2.1B to the healthcare system ($10-20K/procedure)

- However, cystine stones are resistant to this lithotripsy procedure given the strong affinity of cystine dimerization bond
  - Dimer is composed of 2 cysteine residues bound by a disulfide bond
  - Cystine is not readily soluble and accumulation leads to formation of cystine stones
  - Mutations in SLC3A1 and SLC7A9 are identified to impact transporters of cystine, ornithine, lysine and arginine in the kidney



- If left untreated, cystinuria pts can have up to 5 stone events/year, and in the long term, can cause major renal damage, potentially culminating in loss of kidney function

- Most notably, kidney stones are characterized as extremely painful, and hence result in significant loss of productivity and diminished quality of life

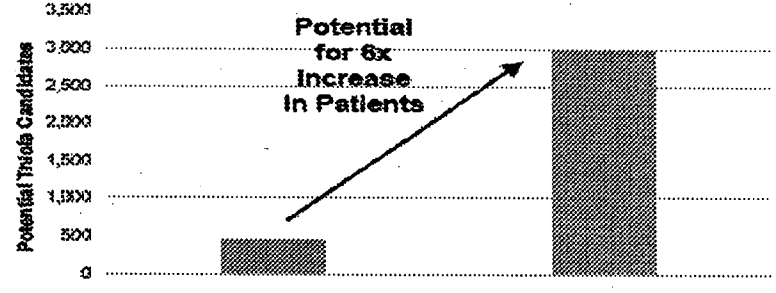
Source: Leerink Partners Research, Company Reports

Sensible Commercial and Development Tactics In Place To Maximize Sales Potential and Drug Exclusivity

LEERINK

- Original manufacturer was primarily responsible for the failed commercialization, including:
  - lack of product supply for 2-3 mos. preceding RTRX's acquisition of the product in May 2015
  - no active sales force; relied on contracts or physicians/patients approaching the company
  - Under-appreciation of the ability to develop a significant potential market opportunity

- Under RTRX, product supply has now been fully restored with a number of commercial tactics in place to maximize Thiola's market opportunity
  - results-driven execution from a dedicated field force and physician/patient support services have driven the number of pts on Thiola from ~250 in 3Q14 to a total of ~650 in Feb. 2015
  - recent market research studies suggest the target patient population may be 4-5K in the U.S., 30-40% higher than RTRX's original estimates of ~3-4K
  - ~30X price increase post-acquisition with Thiola now priced at ~$85K gross per patient per year



- While Thiola doesn't have any patent protection or exclusivity, mgmt remains committed to its closed distribution network to fend off generic threat as no product may be available to conduct bioequivalent studies
  - additional LCM plans include developing a long-acting version of Thiola

Source: Leerink Partners Research, Company Reports

~$150MM Market Oppty Assumes Uptake to Peak at ~2.2K Pts (55% Market Share) on Thiola in 2021; Remaining 45% Is Upside

LEERINK

Cystinuria Revenue Model	1H14E	3Q14E	4Q14E	2014	1Q15E	2Q15E	3Q15E	4Q15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total Cystinuria pts in the US	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000
% with uncontrolled cystine stones	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
Market Penetration		7%	13%	10%	16%	18%	20%	22%	19%	29%	35%	40%	45%	50%	55%	41%	27%	15%	7%	4%	2%	1%
Total Cystinuria pts on Thiola		280	520	520	640	720	800	880	880	1,160	1,400	1,600	1,800	2,000	2,200	1,650	1,073	590	295	147	74	37
Annual Cost of Therapy ($)		21,250	21,250	85,000	21,250	21,250	21,250	21,250	85,000	85,000	85,000	85,000	85,000	85,000	85,000	85,000	85,000	85,000	85,000	85,000	85,000	85,000
US Thiola Gross Revenues ($MM)		6.0	11.1	17.0	13.6	15.3	17.0	18.7	64.6	98.6	119.0	136.0	153.0	170.0	187.0	140.3	91.2	50.1	25.1	12.5	6.3	3.1
US Thiola Net Revenues ($MM)		4.8	8.8	13.6	10.9	12.2	13.6	15.0	51.7	78.9	95.2	108.8	122.4	136.0	149.6	112.2	72.9	40.1	20.1	10.0	5.0	2.5

Thiola Price after RTRX acquisition in May '14	$85,000

Source: Company Reports, Leerink Partners Research

Chenodal for Treatment of Cerebrotendinuous Xanthomatosis (CTX)

CHENODAL™

Highly Accretive Addition of Chenodal in CTX Indication, Including a 5X Price Increase Post-Acquisition

LEERINK

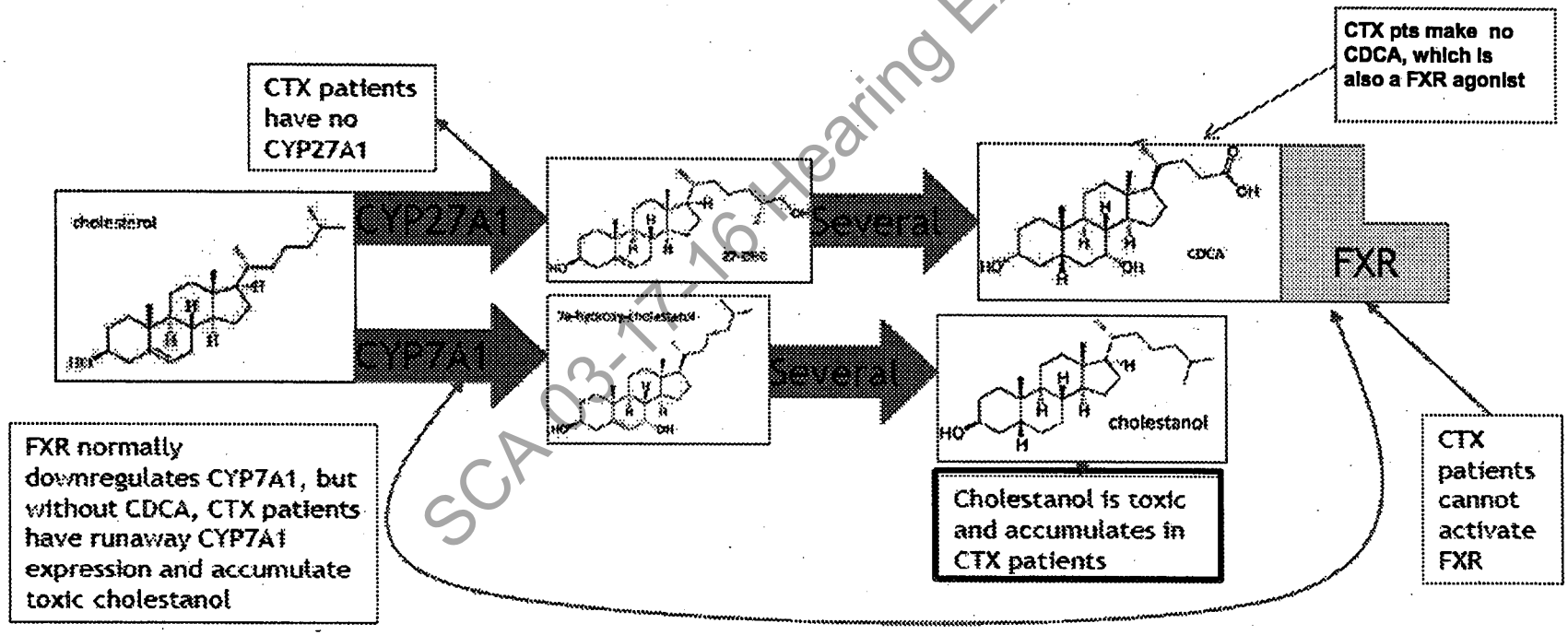
- Chenodal (chenodeoxycholic acid/CDCA) is a synthetic bile acid exclusively used off-label as standard of care for Cerebrotendinuous Xanthomatosis (CTX)
  - Originally approved in 2009 for treatment of gallstones, although there are no sales in that indication
- Chenodal was never subjected to a clinical trial for CTX given its off-label discovery of efficacy and that a clinical trial would be unethical
  - The FDA requested that the manufacturer make Chenodal available for patients who had no other treatment options
  - Based on interactions with the FDA to date, RTRX believes that generation of new clinical data may not be required for label expansion to include CTX
- RTRX recently increased the WAC to $515,000 after recognizing the true clinical potential of Chenodal in CTX
  - Original developer Manchester Pharmaceuticals had priced the drug at ~$110,000 PPY based on the gall stones opportunity
- Official FDA approval in CTX is possible in 1H15, which should further facilitate payer engagement and patient identification efforts
  - Orphan Drug Exclusivity to potentially add 7 years to loss of exclusivity

Source: Leerink Partners Research, Company Reports

CTX Is Caused by an Inborn Error in Metabolism (Lacks CDCA) and Requires Functional Curative Therapy from Chenodal (CDCA)

LEERINK

- CTX is an autosomal recessive metabolism disorder caused from mutation in CYP27A, which is an enzyme that converts cholesterol to CDCA
  - CDCA binds to FXR and downregulates CYP7A1, which generates bile acids from cholesterol
  - Downregulated CDCA in CTX pts result in accumulation of toxic substrates such as cholestanol (healthy subjects have little-to-no serum cholestanol)



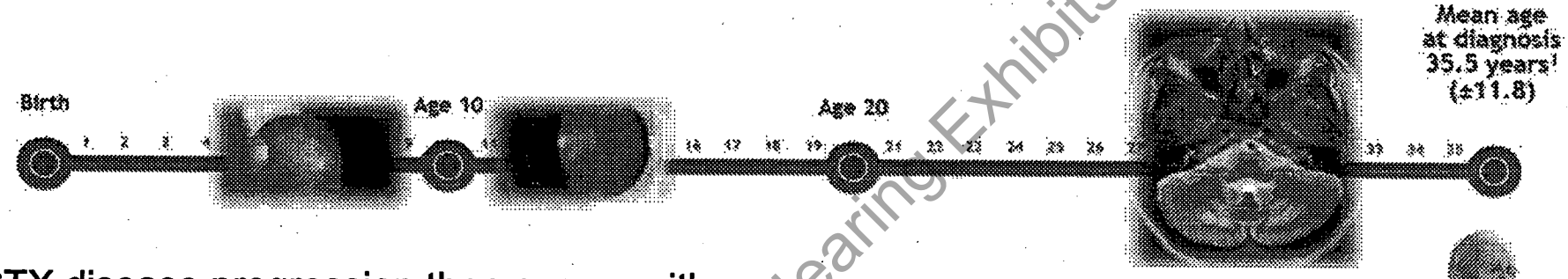
- **Cholestanol drop of ~98% observed following Chenodal Replacement treatment**

Source: Leerink Partners Research, Company Reports

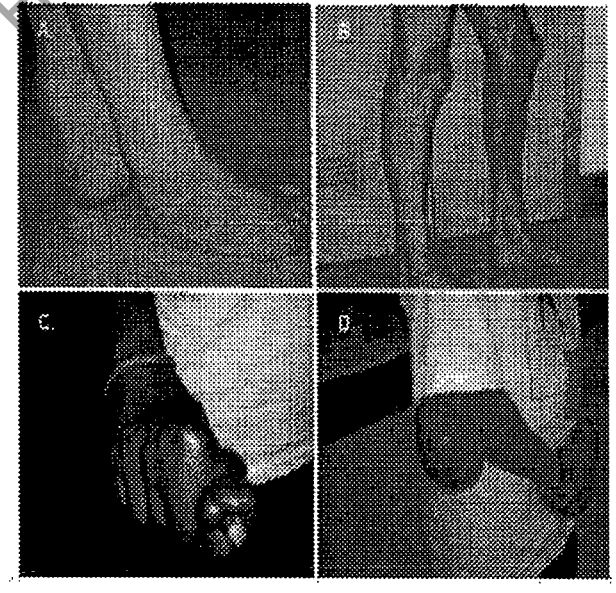
Disease Discovered Originally by Accident, Standard-of-Care Status for Chenodal Now Unquestionable; However, Diagnosis Remains a Challenge

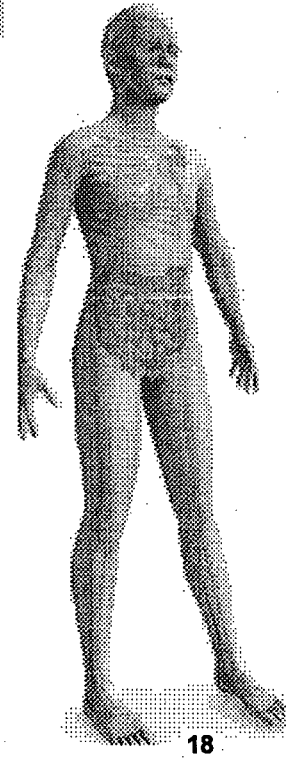
LEERINK

- CTX pts begin life with neonatal cholestatic jaundice and refractory diarrhea, and very rarely do these common, non-critical and non-specific symptoms lead to diagnosis



- CTX disease progression then occurs with juvenile cataracts, tendon xanthomas (lipid deposition), and neurological deterioration (including motor dysfunction and intellectual disabilities)





- Diagnosis generally occurs in pts in their mid-30's after significant neurological damage

- CTX considered by KOLs to be lethal without Chenodal treatment

Source: Leerink Partners Research, Company Reports

Patient Identification Is Key To Achieving Full Potential of the Asset, to Which RTRX Seems To Be Strategically Investing Resources

LEERINK

- Due to under-diagnosis or misdiagnosis of CTX, epidemeology data are limited
  - According to RTRX, there are at least 500-1,000 pts in US, with currently <5-10% diagnosed/treated

- Classic commercial tactics in form of newborn genetic screening, establishing patient registry and increasing physician/patient awareness are being actively pursued
  - Identification of CTX patients is challenging, which combined with increased mortality rates leads us to project conservative net new patient growth for Chenodal in our model

- Major new efforts underway to educate pediatric ophthalmologists to raise awareness in order to facilitate earlier diagnosis since juvenile cataracts are a sentinal symptom
  - RTRX liaising with 35 US ophthalmology centers to screen ~250-500 pts with bilateral cateracts
  - Patients will be referred to molecular geneticists in order to rule out other causes/rule-in CTX
  - Initial results of screening program may become visible to investors by year-end 2015

Source: Leerink Partners Research, Company Reports

~$50MM Peak Revenues Assume Very Conservative Growth Estimates of Chenodal Given the Uncertainty in Diagnosis

LEERINK

- RTRX has been working on converting ~60 pts on commercial drug with revised pricing of $515K per patient per year
- Extensive screening efforts are likely to translate into a considerable increase in total CTX pts diagnosed; however, we assume a very conservative increase in our estimates
  - Our 80% peak penetration assumes RTRX effectively engaging with payers, physicians and patients in order to maximize access of Chenodal

Chenodal CTX US Revenue Model	1H14E	3Q14E	4Q14E	2014	1Q15E	2Q15E	3Q15E	4Q15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total CTX pts in the US	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
% Diagnosed	10%	10%	10%	10%	10%	10%	10%	11%	10%	11%	11%	12%	12%	13%	13%	14%	14%	15%	15%	16%	16%	17%
Market Penetration		30%	40%	40%	45%	50%	55%	65%	68%	70%	73%	75%	78%	80%	80%	80%	68%	58%	49%	42%	35%	30%
Total CTX pts on Chenodal		30	40	40	46	51	57	68	68	76	82	89	95	103	107	111	97	86	75	66	58	51
Annual Cost of Therapy		128,750	128,750	515,000	128,750	128,750	128,750	128,750	515,000	515,000	515,000	515,000	515,000	515,000	515,000	515,000	515,000	515,000	515,000	515,000	515,000	515,000
US Gross Revenues ($MM)		3.9	5.2	9.0	5.9	6.6	7.3	8.8	28.6	39.0	42.2	45.6	49.1	52.8	54.8	56.9	50.1	44.1	38.7	34.0	29.8	26.1
US Chenodal Net Revenues ($MM)		3.4	4.5	7.8	5.1	5.7	6.4	7.6	24.9	33.9	36.7	39.7	42.8	45.9	47.7	49.5	43.6	38.4	33.7	29.6	25.9	22.7

Source: Company Reports, Leerink Partners Research

Note: Likely upside revisions pending more visibility into results from ongoing screening efforts and potential development of a diagnostics by YE15

Source: Leerink Partners Research, Company Reports

Cholbam for the Treatment of Rare Bile Acid Disorders

Asklepion Acquisition in Jan. '15 Generated Significant Shareholder Value With Cholbam's Approval in March '15 Accompanied by an Unexpected PRV

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FDA News Release

FDA approves Cholbam to treat rare bile acid synthesis disorders

For Immediate Release March 17, 2015

- **The efficacy of Cholbam for the treatment of patients with bile acid synthesis disorders due to single enzyme defects was assessed in a single arm trial involving 50 patients treated over an 18 year period. An extension trial followed 21 of these patients and enrolled an additional 12 patients with interim efficacy data available for an additional 21 months.**
  - On average, patients were 4 years of age at the start of cholic acid treatment (range 3 weeks to 36 years).
  - Response to treatment was evaluated by improvements in baseline liver function tests and weight. Responses were noted in 64 percent of patients with evaluable data.
  - Two-thirds of patients survived greater than 3 years. Literature reports also supported the efficacy of Cholbam in this population.

- **The efficacy of Cholbam for the treatment of peroxisomal disorders, including Zellweger spectrum disorders, was assessed in a single arm, treatment trial involving 29 patients treated over an 18 year period. An extension trial followed 10 of these patients and enrolled an additional two patients with interim efficacy data available for 21 additional months.**
  - The majority of patients were less than 2 years of age at the start of cholic acid treatment (range 3 weeks to 10 years).
  - Response to treatment was evaluated by improvements in baseline liver function tests and weight. Responses were noted in 46 percent of patients with evaluable data.
  - Forty-two percent of patients survived greater than 3 years.

Posted on FDA's website on March 17th 2015

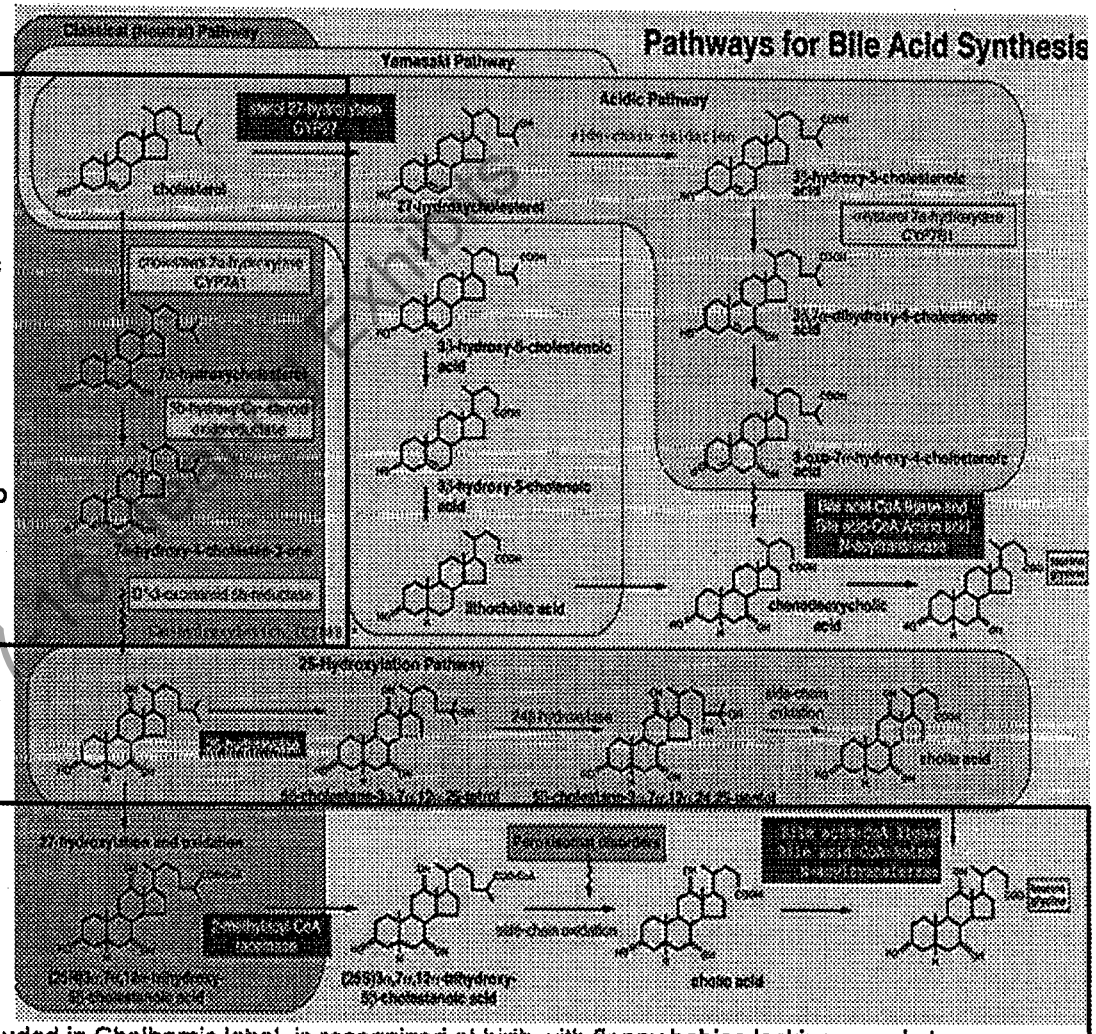
Bile Acid Synthesis Disorders Categorized As: Monogenic Largely in Adults (chronic & ultra-rare) and Peroxisomal in Pediatrics (fatal & more prevalent)

LEERINK

~40-350 adult + pediatric pts in US needing chronic treatment

Monogenic defects in the synthesis pathway results in production and accumulation of abnormal and hepatotoxic/cholestatic bile acid precursors

- Build up of defective bile acids lead to highly symptomatic conditions such as cholestasis, nutrient malabsorption, liver disease, neurologic disease, and, eventually, liver failure and death
- Majority of cases go undiagnosed and untreated
- Prevalence is very broadly estimated to be 1 in 1-9M, however the chronic nature of treatment should enable pts to stay on Cholbam therapy for years
- RTRX may have ~20-30 pts on treatment by YE15 and is expected to initiate a US registry study in order to genetically screen patients eligible to receive Cholbam



~7K pediatric pts, typically newborns, needing relatively short-term treatment

Peroxisomal disorders are characterized by lack the key liver enzymes at birth that are responsible for breakdown of long chain fatty acids (through beta-oxidation) leading to numerous problems in multiple organ systems (brain, lung, kidney etc.)

- Zeilweger spectrum disorder, a kind of peroxisomal disorder also included in Cholbam's label, is recognized at birth with floppy babies lacking muscle tone
- The functionality of Cholic acid is disrupted with long lipid side chains thereby making the final product toxic to the liver
- Prevalence is relatively bigger with 1 in 50K; however, longevity is not significantly improved as Cholbam primarily improves hepatic function and not any other severe abnormalities around neurological and kidney function
- RTRX has identified ~20-30 pts at launch, with the goal to identify ~30 new pts every year

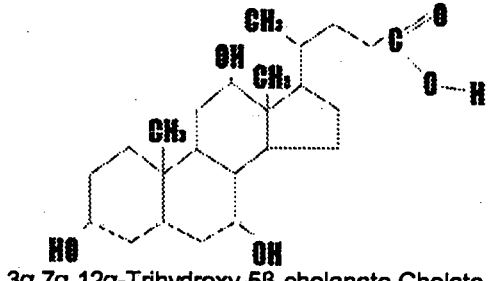
Source: Company Reports, Leerink Partners Research, Fischier et al.

Cholbam Has an Opposite Action to That of Cholesterol in Inhibition of Production of Atypical Toxic Bile Acids, Which In Turn Improves Liver Function

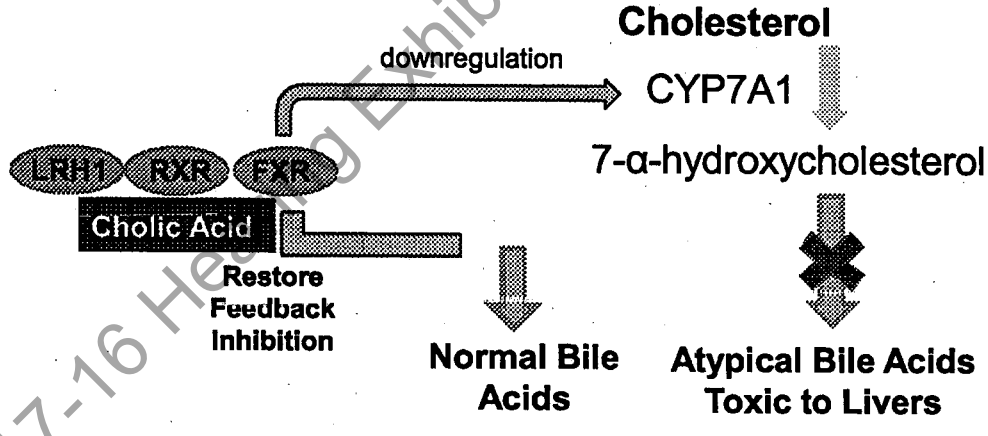
LEERINK

- Cholbam, also referred to as cholic acid, is characterized to:
  - be a primary bile acid on which essential physiological functions depend such as digestion of fats, cholesterol homeostasis, absorb fat-soluble vitamins and has shown antibacterial activity
  - downregulate cholesterol-7-α-hydroxylase, which is the rate limiting step in bile acid synthesis

Cholic Acid



3α,7α,12α-Trihydroxy-5β-cholanate Cholate
$C_{24}H_{40}O_5$



- 20-year, open label, single-arm, IIT (investigator-initiated trial) at Cincinnati Children's Hospital & Medical Center warranted Cholbam's approval in pts with bile acid deficiency disorders
  - 64% (28/44) Response Rate in pts with single-enzyme defects
  - 46% (11/24) Response Rate in pts with peroxisomal disorders
- Some patients have been on Cholbam for ≥18 years exhibiting:
  - Normal liver function as shown by improved liver function test values
  - Restoration of growth, as assessed by weigh gain in comparison to natural history of untreated pts
  - Benign safety profile, which is particularly important for chronic treatment in pts single-enzyme defects

Single Enzyme Defect	Response Rates
CTX	100% (2/2)
AMACR	100% (1/1)
AKR1D1	75% (3/4)
3β-HSD	59% (22/37)
AMACR	

Peroxisomal Disorder	Response Rates
Zellweger Syndrome	100% (1/1)
Generalized Peroxisomal Disorder	100% (1/1)
Refsum Disease	75% (3/4)
Neonatal Adrenoleukodystropyhy	50% (3/6)
CYP7A1	38% (3/8)
Peroxisomal Disorder, Type Unknown	20% (1/5)

Source: Cholbam Label, Leerink Partners Research, Setchell et. al.

$150MM Peak Sales Assume Cautious Estimates on Rate of Patient Identification in Both Monogenic & Peroxisomal Subgroups

LEERINK

- At peak in 2025, we assume ~130 monogenic and ~380 peroxisomal patients on Cholbam in US
  - Share of EU as a percentage of US patient population is assumed to peak at <50%
- While Cholbam's price remains to be finalized, we expect Cholbam to be priced roughly at parity with Chenodal while also taking into account the cost per mg basis as on an average Cholbam pts are relatively smaller and younger.
  - We assume average weight of 45 kg and 15 kg for monogenic and peroxisomal pts, respectively
  - EU price is assumed to be ~70% of the US WAC price

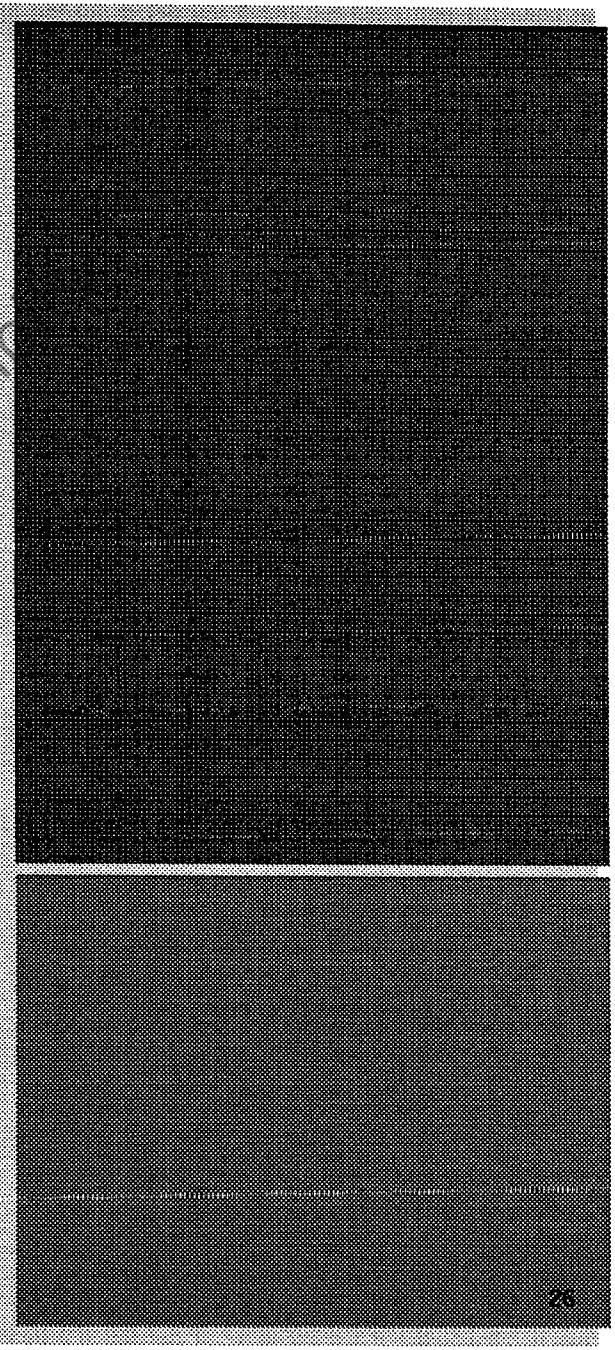
Rare Bile Acid Disorders US Revenue Model ($MM)	1Q14E	2Q14E	3Q14E	4Q14E	2014E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total RBA pts in the US	7,100	7,136	7,172	7,209	7,245	7,286	7,327	7,369	7,411	7,454	7,497	7,541	7,585	7,630	7,676	7,722	7,768	7,816
Monogenic (adults + pediatric; chonic)	100	101	102	103	104	109	115	120	126	133	139	146	154	161	170	178	187	196
Market Penetration		20%	25%	30%	25%	35%	40%	45%	50%	55%	60%	65%	70%	75%	75%	49%	32%	21%
Total Monogenic RBA Pts on Cholbam	-	20	26	31	26	38	46	54	63	73	84	95	108	121	128	87	60	41
Peroxisomal (pediatric; 1-2 yrs longevity)	7,000	7,035	7,070	7,106	7,141	7,177	7,213	7,249	7,285	7,321	7,358	7,395	7,432	7,469	7,506	7,544	7,581	7,619
Market Penetration	0.3%	0.3%	0.4%	0.4%	0.4%	0.5%	0.7%	1.1%	1.6%	2.4%	2.9%	3.5%	4.2%	4.6%	5.1%	3.3%	2.2%	1.4%
Total Peroxisomal pts on Cholbam	21	23	26	28	31	35	52	79	119	179	216	260	314	347	384	251	164	107
Annual Cost of Therapy ($/kg)	2,778	2,778	2,778	2,778	11,111	11,111	11,111	11,111	11,111	11,111	11,111	11,111	11,111	11,111	11,111	11,111	11,111	11,111
US Gross Revenues	0.9	3.5	4.3	5.0	18.2	24.9	31.7	40.2	51.4	66.4	77.8	91.0	106.2	118.4	127.9	85.4	57.1	38.1

Rare Bile Acid Disorders EU Revenue Model ($MM)	1Q15E	2Q15E	3Q15E	4Q15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
EU Monogenic RBA pts on Cholbam (% of US)						*20%*	*22%*	*24%*	*27%*	*29%*	*32%*	*35%*	*39%*	*43%*	*47%*	*31%*	*20%*	*13%*
EU Peroxisomal RBA pts on Cholbam (% of US)						*20%*	*22%*	*24%*	*27%*	*29%*	*32%*	*35%*	*39%*	*43%*	*47%*	*31%*	*20%*	*13%*
Annual Cost of Therapy ($/kg)						8,333	8,333	8,333	8,333	8,333	8,333	8,333	8,333	8,333	8,333	8,333	8,333	8,333
EU Gross Revenues						3.7	5.2	7.3	10.3	14.6	18.8	24.2	31.0	38.1	45.2	19.6	8.5	3.7
WW Cholbam Gross Revenues ($MM)	0.9	3.5	4.3	5.0	18.2	28.6	36.9	47.5	61.7	80.9	96.6	115.2	137.2	156.5	173.1	105.0	65.6	41.8
WW Cholbam Net Revenues ($MM)	0.7	3.0	3.6	4.3	15.5	24.3	31.3	40.4	52.4	68.8	82.1	97.9	116.6	133.0	147.1	89.3	55.7	35.6

Cholbam US Price at launch ($/kg)	$11,111
Cholbam EU Price at launch ($/kg)	$8,333
Average Weight For Monogenic (kg)	45
Average Weight For Peroxisomal (kg)	15

Source: Company Reports, Leerink Partners Research

Sparsentan for Treatment of Focal Segmental Glomerulosclerosis (FSGS)



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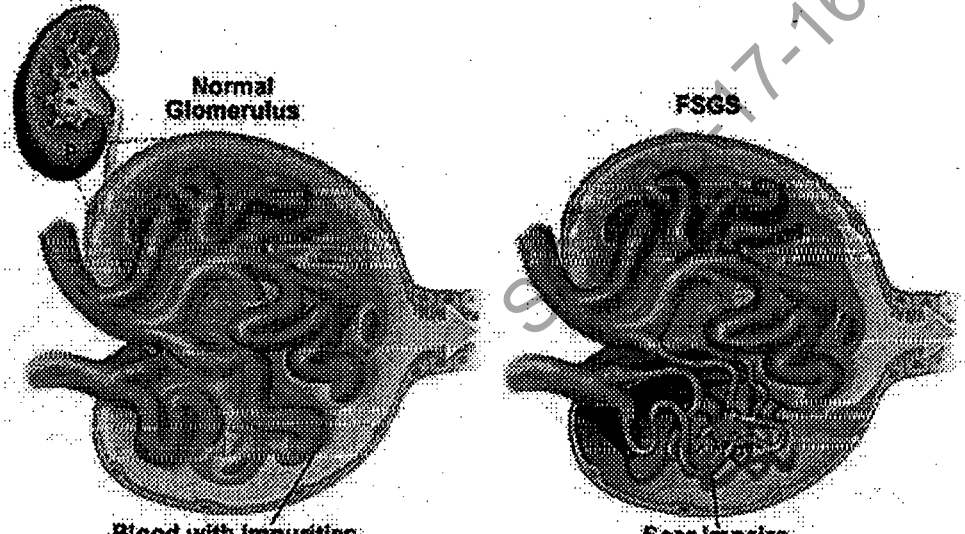
In FSGS, Some Sections of Kidney Filters ("Glomeruli") Are Scarred

- Focal segmental glomerulosclerosis (FSGS) is a leading cause of nephrotic syndrome in children and adolescents, as well as kidney failure in adults. It accounts for about a sixth of the cases of nephrotic syndrome, and is the most common cause of steroid-resistant nephrotic syndrome in children. It is the second leading cause of kidney failure in children.
- The individual components of the name refer to the appearance of kidney tissue on biopsy: *focal* - only some of the glomeruli are involved (as opposed to diffuse), *segmental* - only part of each glomerulus is involved (as opposed to global), *glomerulosclerosis* - refers to scarring of the glomerulus (a part of the nephron, the functional unit of the kidney).
- FSGS is usually indicated by heavy PAS staining on biopsy histology and findings of IgM and C3 in sclerotic segments. Each kidney contains ~1MM filters called glomeruli, which are impaired in FSGS as shown in the schematic and biopsy histology below:



Source: www.nephcure.org

Source: Schwimmer, J. et. al. Collapsing Glomerulopathy. Seminars in Nephrology. March 2003: Vol 23, Issue 2

FSGS Pathophysiology Has Become Better Understood and the Disease Has Become More Commonly Diagnosed

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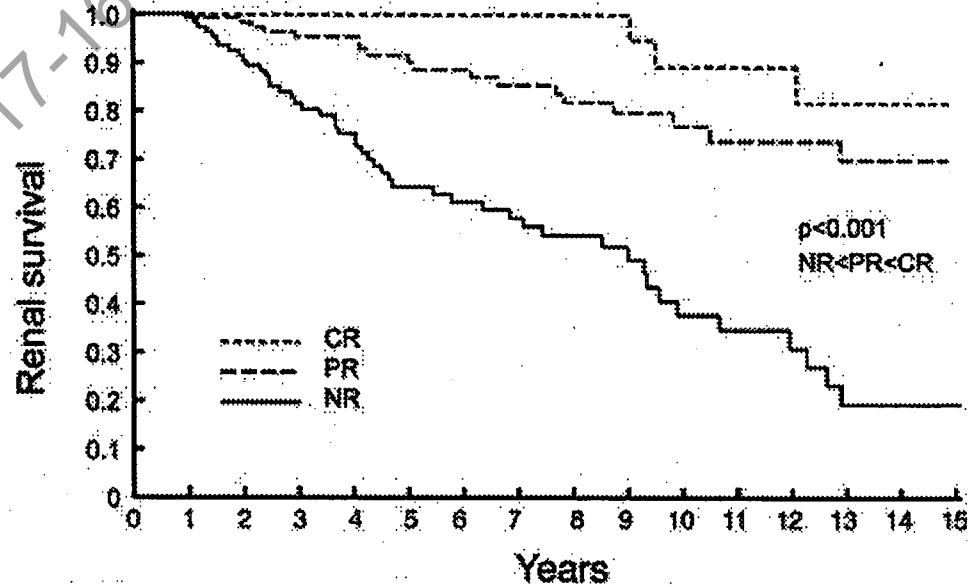
- FSGS may be secondary to other disease processes such as sickle cell, obesity, other drugs, and HIV, although 80% of FSGS cases are due to unknown causes and considered idiopathic.
- The renal glomerulus filters the blood that arrives at the kidney. It is formed of capillaries with small pores that allow small molecules to pass through but not larger macromolecules such as proteins. In nephrotic syndrome, the glomeruli are affected by an inflammation or a hyalinization process (the formation of a homogenous crystalline material within cells) that allows proteins such as albumin, antithrombin or the immunoglobulins to pass through the cell membrane and appear in urine. Albumin is the main protein in the blood that is able to maintain an oncotic pressure, which prevents the leakage of fluid into the extracellular medium and the subsequent formation of edemas.
- In children and some adults, FSGS presents as a nephrotic syndrome, which is characterized by edema (associated with weight gain), hypoalbuminemia (low serum albumin, a protein in the blood), hyperlipidemia and hypertension (high blood pressure).
- In adults, FSGS may also present as kidney failure and proteinuria, without a full-blown nephrotic syndrome. Heavy proteinuria portends a poor long-term outcome.
- **The total prevalence of FSGS is estimated at 25-50k in the U.S.** Nephcure estimates that 19k patients are living with ESRD caused by FSGS in the US. United States Renal Data Service estimates that FSGS accounts for more than 7k patients currently receiving ESRD therapy in the United States, and it is likely that primary FSGS accounts for some of the 25k patients with unspecified forms of glomerulonephritis, 100k patients with ESRD attributed to hypertension, and 20k patients with unknown cause of ESRD.

Sparsentan in FSGS – Rationale for Study and Potential Accelerated Approval

- The goal of FSGS therapy is to induce a complete or partial remission of proteinuria and preserve renal function. Even partial remission is associated with improved long-term survival. Treatment of primary focal segmental glomerulosclerosis is empiric and based on the rationale that different patients have different dysregulated immune systems.
- Current treatment includes salt restriction and diuretics, such as furosemide, for edema. This is soon followed by antihypertensives (ACEIs/ARBs) and lipid lowering drugs. Aldosterone antagonists are often used to decrease proteinuria and offer renal protection. Corticosteroids such as prednisone and cytotoxics such as cyclophosphamide may be used to induce remission. Other immunosuppressive drugs are generally the drug treatment of last resort before patients require dialysis and potentially kidney transplantation.
- **As with other serious renal diseases such as lupus nephritis and diabetic nephropathy, slowing the rate of progression to end stage renal disease (ESRD) may be an acceptable registrational endpoint for approval by FDA/EMEA.** Natural history data shows that increasing rates of reductions in proteinurea results in increasing rates of dialysis-free survival.



Source: Troyanov, S. et al. J Am Soc Nephrol 16: 1061-1068, 2005

Sparsentan in FSGS – Mechanism of Action Is a Logical Hypothesis to Test

- **Retrophin is developing the dual endothelin-receptor A/ARB RE-024/Sparsentan in patients with FSGS.**
  - **Endothelin receptor antagonists have shown the ability to reduce blood pressure and proteinurea in several settings.**
  - **Angiotensin-receptor blockers are commonly used in patients with hypertension and diabetic nephropathy. Irbesartan has trial data showing benefit in hypertensive patients with type II diabetes, and may delay the progression of diabetic nephropathy.**
  - Licensor Ligand Pharmaceuticals is entitled to a royalty of 9% on sales of Sparsentan.
- The kidney is an important site of endothelin-1 (ET-1) production and is particularly susceptible to ET-1 action.
  - Infusion of ET-1 in rats induces both functional and morphological alterations in the kidneys. Increased plasma level of ET-1 has been reported in patients with chronic renal failure.
  - Studies have shown that plasma ET-1 concentration in FSGS patients was significantly higher than in normal controls ($P < 0.05$), and that urinary ET-1 excretion rate was also significantly higher in FSGS patients than in normal controls ($P < 0.01$).
  - In FSGS patients, plasma and urinary ET-1 have been shown to be significantly correlated ($P < 0.05$), and the urinary ET-1 excretion rate was significantly correlated with the amount of proteinuria ($P < 0.05$) and the glomerular sclerosing score ($P < 0.01$).

Source: Leerink Partners research, Company filings, Chen HC et al. J Clin Lab Anal. 2001;15(2):59-63.

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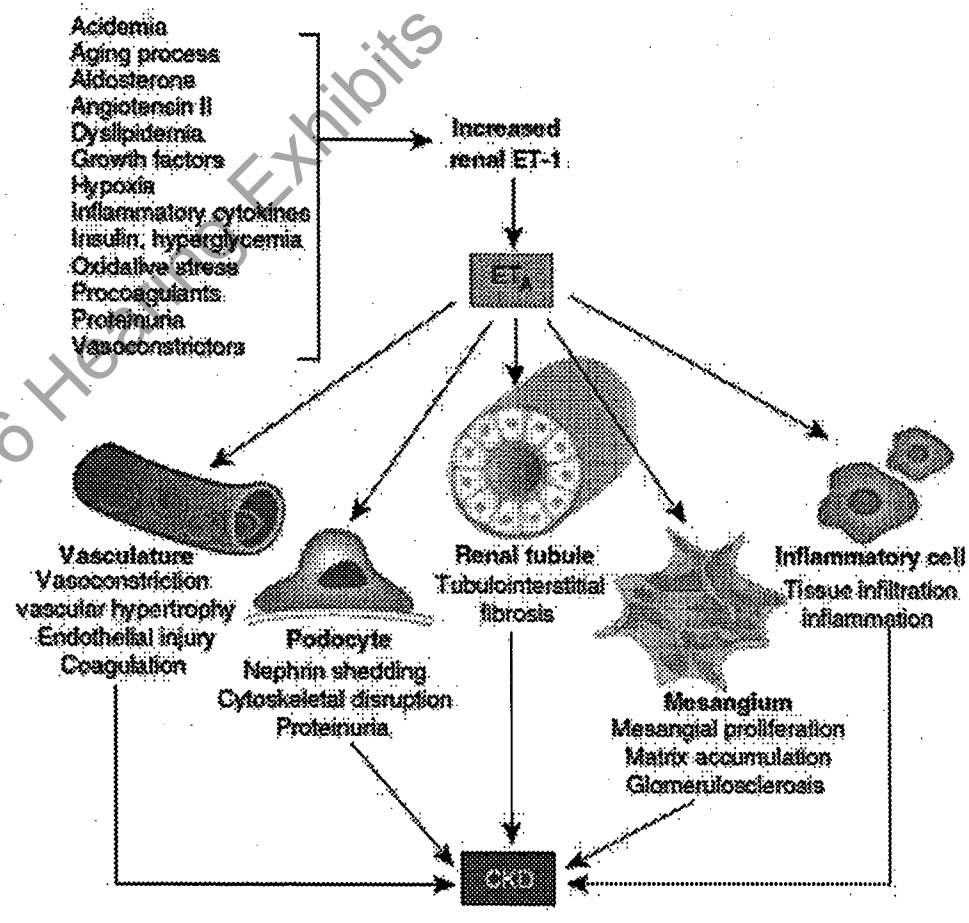
Sparsentan in FSGS – MOA Targeted Against ET_A (and Not ET_B)… Plus an ARB

- Endothelin (ET) is a peptide present in virtually every cell in the body, especially the vasculature, where it acts as an extremely potent vasoconstrictor. ETs bind to two receptor isoforms: ET_A and ETB.
- **Based on the role of the renal tubular ET_B receptor in mediating sodium excretion, and experience of ET blockers to date, less edema is expected by only targeting ET_A.**
- In addition to actions on vascular tone, ETs also promote growth and proliferation of vascular smooth muscle cells, an effect that appears to be ET_A receptor-mediated. There is also direct and indirect evidence suggesting that ETs stimulate oxidative stress in the vasculature, an effect that some studies have attributed primarily to the ET_A receptor.
- ET_A is believed to promote vasoconstriction, cell proliferation and matrix accumulation; ET_B activation is vasodilatory, antiproliferative, and antifibrotic. ET_B receptor function is also believed to be critical for clearing endothelin.
- Renal ET is an important regulator of renal sodium and water retention. Volume loading increases nephron ET production, which inhibits sodium and water reabsorption. ET_A also appears to exert a naturiuretic effect, but these exact mechanisms are still unclear.



Source: Kohan, D. and Barton, M. Endothelin and Endothelin Antagonists in Chronic Kidney Disease. Kidney International. May 7, 2014

Other ETRAs Have Shown Antiproteinuric Effects in Other Nephropathic Syndromes, But Nonspecific ETRAs Have Been Hampered by Fluid Retention/Edema

LEERINK

- Despite available therapies, many FSGS patients have nephrotic range proteinuria, and new therapeutic agents are needed (Kiffel, et al., 2011). **As shown below, endothelin receptor antagonists (ETRAs) have been shown to lower proteinuria in clinical trials of diabetic nephropathy (Kohan, et al., 2011) (Mann, et al., 2010) but less selective ETRAs have been associated with more significant fluid retention which is problematic for kidney disease pts.**

Disease	Study type	Drug	Size	Outcome	Comments
Hypertensive nephropathy	Acute infusion	BQ123 (ET_A) BQ788 (ET_B)	$N = 16$	BQ123 increased renal blood flow—prevented by BQ788	BQ123 response seen in CKD, but not in healthy patients.
Nondiabetic CKD	Acute infusion	BQ123 (ET_A)	$N = 22$	BQ123 reduced proteinuria and pulse wave velocity > nifedipine	Reduction in proteinuria and pulse wave velocity partly independent of blood pressure effects
Nondiabetic CKD	Acute infusion	TAK-044 ($ET_A/_B$)	$N = 7$	TAK-044 tended to increase renal blood flow	Compared with placebo, TAK-044 reduced blood pressure and increased cardiac index
Diabetic nephropathy	Phase 2	Avosentan (ETA:B 50-300:1) 5, 10, 25, 50 mg/d	$N = 286$	Avosentan reduced UACR by ~21—30% from 5-50 mg/d vs. ~35% increased UACR in placebo	Baseline CrCl ~80 ml/min, UAER ~1500 mg/d. Fluid retention dose-dependent, ranging from 12-32% of patients.
Diabetic nephropathy	Phase 3 (ASCEND)	Avosentan (ETA:B 50-300:1) 25, 50 mg/d	$N = 1392$	44-49% reduction in UACR after ~4 months in avosentan group, 9% reduction in placebo	Baseline median eGFR ~33 ml/min/1.73 m^2, median UACR ~1500 mg/g. Trial terminated owing to adverse events related to fluid retention
Nondiabetic CKD	Phase 2	Sitaxsentan (ET_A) vs. nifedipine	$N = 27$	Sitaxsentan, but not nifedipine, reduced proteinuria after 6 weeks	CKD stages 1-4
Diabetic nephropathy	Phase 2a	Atrasentan (ET_A) 0.25, 0.75, 1.75 mg/d	$N = 89$	Atrasentan reduced UACR ~35-40% at two highest doses vs. 11% decrease in placebo	Baseline UACR 350-515 mg/g and eGFR 48-61 ml/min/1.73 m^2. Edema dose-dependent (14-46%) and generally mild
Diabetic nephropathy	Phase 2b (RADAR)	Atrasentan (ET_A) 0.75, 1.25 mg/d	$N = 211$	Atrasentan reduced UACR ~35-39% vs. no change in placebo	Baseline eGFR 30-75 ml/min/1.73 m^2, UACR 300-3500 mg/g, taking MTLD ACEI or ARB. Edema similar between groups
Diabetic nephropathy	Phase 3 (SONAR)	Atrasentan (ET_A) 0.75 mg/d	Projected ~4150	Actively enrolling. Primary end point—time to serum creatinine doubling or ESRD.	Baseline eGFR 25-75 ml/min/1.73 m^2, UACR 300-5000 mg/g, taking MTLD ACEI or ARB.
Diabetic nephropathy	Phase 2	Daglutril (ECE inhibitor)	$N = 45$	No change in UAER after 8 weeks	Baseline GFR ~70-90 ml/min, UAER 20-999 µg/min. All taking losartan 100 mg/d.
Primary FSGS	Phase 2	RE-021 (dual ET_A inhibitor and ARB)	$N = 72$	Not yet started. Primary end point—reduction in proteinuria.	Baseline eGFR >45 ml/min/1.73 m^2, ages 8-50 years.

Source: Kohan, D. and Barton, M. Endothelin and Endothelin Antagonists in Chronic Kidney Disease. Kidney International. May 7, 2014

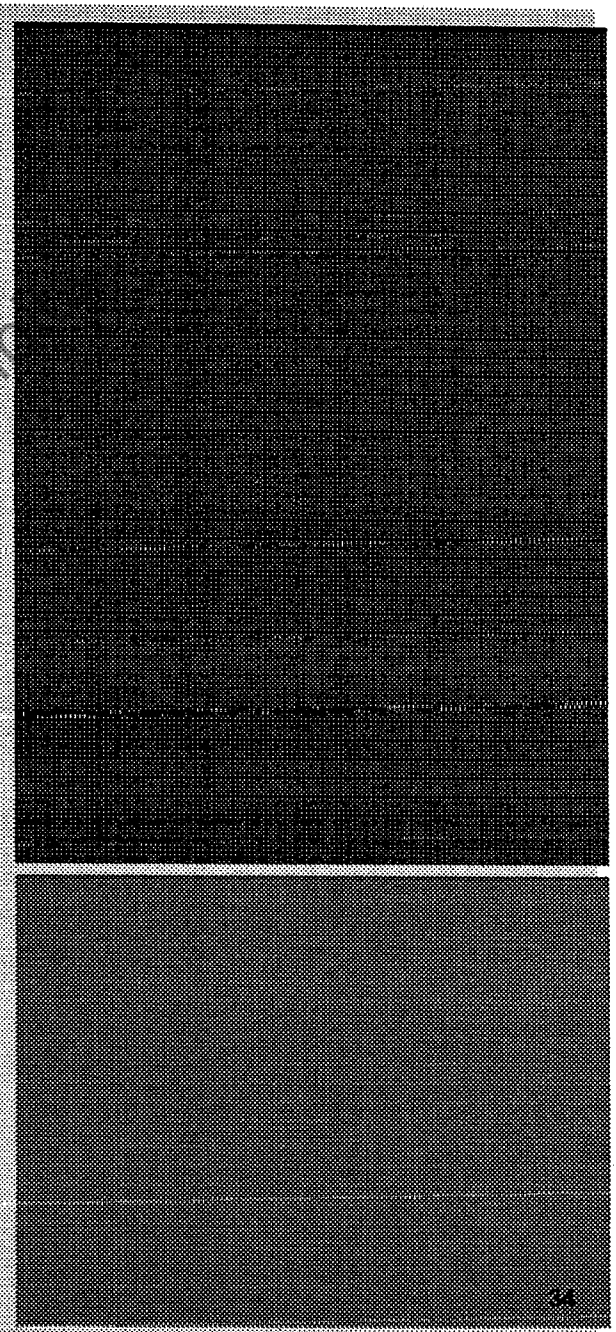
Sparsentan in FSGS – Ongoing Phase II DUET Study Expected To Complete Enrollment by YE15 and Report Data in Mid-2016

LEERINK

- 100 patients are being randomized to one of three doses (200mg, 400mg or 800mg/day) of RE-021 (Sparsentan) or treatment with irbesartan as an active control.
- **The Primary endpoint is the change in urine protein/creatinine (Up/C) after 8 weeks.**
- Secondary endpoints are LDL reduction, Serum albumin, Weight change, Quality of life
- Over 500 patients have received Sparsentan in clinical studies run by Bristol-Myers and Pharmacopeia, so the drug is expected to be well tolerated.
- **A composition of matter patent has been granted that extends until 2019, not including up to 5 years of additional Hatch-Waxman protection/patent term restoration, which may be added.**
- **Retrophin has also been granted orphan drug designation for Sparsentan, which we believe may translate into 7.0-7.5 years of orphan drug exclusivity as well.**
- We project a ~$950MM peak gross market opportunity, and a 65% probability of success.

Sparsentan FSGS Revenue Model	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total FSGS pts in the US	40,000	40,010	40,210	40,411	40,613	40,816	41,020	41,225	41,432	41,639	41,847	42,056	42,266	42,478	42,690
Primary FSGS pts	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Market Penetration					2%	4%	7%	12%	18%	22%	28%	30%	20%	13%	8%
Total FSGS pts on Sparsentan					406	816	1,436	2,474	3,729	4,580	5,859	6,308	4,121	2,692	1,759
Annual Cost of Therapy					150,000	150,000	150,000	150,000	150,000	150,000	150,000	150,000	150,000	150,000	150,000
US Gross Revenues					60.9	122.4	215.4	371.0	559.3	687.0	878.8	946.3	618.1	403.8	263.8
Probability of Success					65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%
US Risk-Adjusted Gross Revenues				-	**39.6**	**79.6**	**140.0**	**241.2**	**363.6**	**446.6**	**571.2**	**615.1**	**401.8**	**262.5**	**171.5**
Source: Company Reports, Leerink Partners Research															

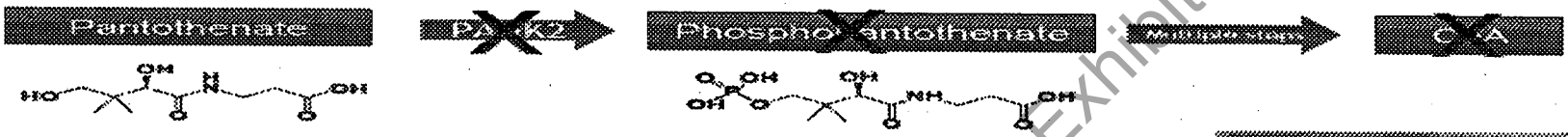
RE-024 for Treatment of Pantothenate Kinase-Associated Neuro-degeneration (PKAN)



PKAN Is a Fatal Ultra-Orphan Hereditary Neurodegenerative Disorder, Primarily Caused by a Missing Enzyme in the CoA Synthesis Pathway

LEERINK

- Pantothenate kinase (PANK2) enzyme is known to phosphorylate its substrate, pantothenate (Vitamin B5) into phosphopantothenate, which is essential to the synthesis of Coenzyme (CoA) metabolism
  - PKAN is an autosomal recessive disorder resulting from the mutation in PANK2 gene responsible for encoding this very critical CoA synthesis enzyme



- Primary symptom is dystonia, a neurological movement disorder, in which sustained muscle contractions cause twisting and repetitive movements or abnormal postures
  - Often initiated or worsened by voluntary movements and symptoms that may "overflow" into adjacent muscles
  - Impaired gait often results into loss of ambulation
  - restricted visual fields diagnosed as retinitis pigmentosa (RP)
- Death prior to the age of 10 is characterized as the most likely outcome of the complications relating to classic PKAN (75% of total pts), which is known for early onset (typically <6 years of age) and rapid progression
  - Atypical onset (25%) is characterized by adult-onset and slower progression
- Eye-of-the-tiger on MRI scans is a key disease characteristic with high-signal intensities surrounding the global pallidus (sub-cortical brain structures), which is representative of iron deposition
  - It remains unclear, however, if progressive iron deposition in the basal ganglia is contributing to disease pathophysiology or merely represents an epiphenomenon

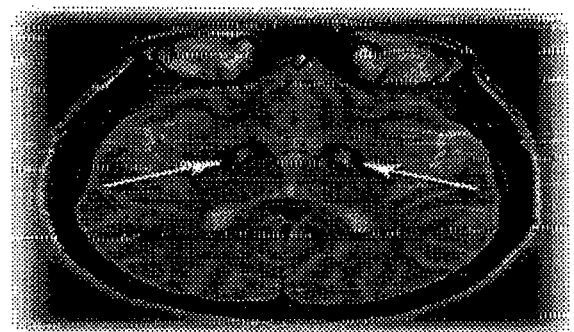


Fig: MRI showing globus pallidus hypointensifying, consistent with iron deposition and supporting diagnosis of PKAN NBIA (neurodegeneration with brain iron accumulation) 35

Source: NBIA Disorders Association, NBIACure.org, Company Reports

Limited Treatment Options Are Available That Largely Provide Very Modest Symptomatic Relief That Is Short-Lived Across Disease Course

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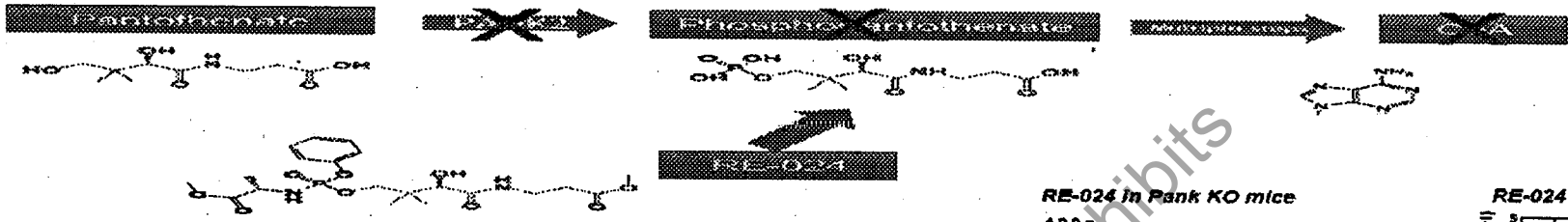
- Typically oral medications are used to treat the extrapyramidal symptoms of the disease including dystonia and parkinsonism (baclofen, trihexyphenidyl, benzodiazepines, and dopamine receptor agonists/antagonists)
  - Even though dystonia is always present in classic PKAN as an early manifestation of the disease, patients do not benefit from Levodopa (L-dopa)
  - Baclofen and trihexyhphenidyl are most effective until the drugs are no longer able to control movement
- More progressive stages of the disease are characterized by treatment with more invasive treatments that can provide some benefit
  - More invasive surgical interventions including placement of an intrathecal baclofen pump and deep brain stimulation have been used to provide some benefit in patients experiencing extreme dystonia and spasticity
  - Even with ablative pallidotomy or thalmotomy, the dystonia will still reappear after an average of one year
  - It is to be noted that all these benefits have a limited time course in most patients
- Interventions are also indicated to treat the retinopathy that occurs in 2/3 of classic PKAN patients
- Patients must also be frequently monitored to prevent complications from fractures, difficulty eating, and visual impairments

Source: Zorzi et al., 2011; Cossu et al., 2014 ; Schipper, 2012

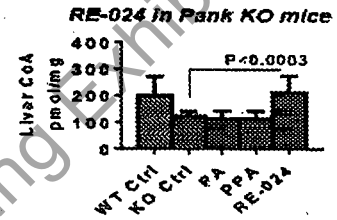
RE-024's Simplistic Mechanism of Substrate Replacement Seems To Be Showing Early (Pre-IND) But Very Promising Efficacy Signal in 2 Ex-US Pts

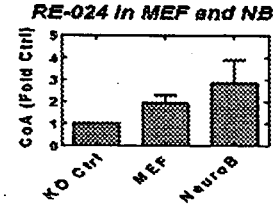
LEERINK

- RE-024 is a small molecule used as a replacement therapy for phosphopantothenate, the missing substrate.



- Preclinical evidence has shown restored CoA levels in PANK KO mice, PANK1 MEF and PANK2 silenced human neuroblastoma cells.





- In 2 pts receiving RE-024 under "compassionate use", disease stabilization reported on several clinical & functional endpoints.

1. **Unified Parkinson's Disease Rating Scale** (widely established regulatory endpoint for Parkinson's)
2. **Barry Albright Dystonia Scale** (measure of dystonia)
3. **Measure of Quality of Life**
4. **Functional Outcome** (25 foot walk test)

	Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 7	Week 11
SUBJECT 1								
UPDRS[1] (A+B+C)	71/118	56/118	56/118	63/118	55/118	56/118	48/118	50/118
Subscale A	8/10	3/10	3/10	3/10	4/10	3/10	2/10	3/10
Subscale B	36/52	26/52	26/52	27/52	26/52	26/52	23/52	22/52
Subscale C	40/56	27/56	27/56	33/56	28/56	27/56	23/56	25/56
BADS[2]	14/24	15/24	14/24	16/24	13/24	14/24	13/24	14/24
EQ-5D-3L	12/15	12/15	10/15	10/15	9/15	9/15	8/15	10/15
25 foot walk test								
# of steps	23.5	19.5	17.0	16.0	16.5	15.0	14.0	14.5
Time in seconds	10.5	11.3	8.6	11.1	8.9	8.2	7.6	7.8

	Week 0	Week 1[3]
SUBJECT 3		
UPDRS (A+B+C)	53/118	36/118
Subscale A	4/10	4/10
Subscale B	23/52	17/52
Subscale C	26/56	15/56
BADS	14/24	13/24

TABLE 3: Biochemical data summary (as of August 11, 2014)

5. **Per physician report, liver enzymes remain within normal limits**

	Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 7	Week 11
SUBJECT 1								
ALT	84	31	85	65	58	35	27	WNL[4]
AST	25	23	35	32	29	30	26	WNL
Lactate	2.44	1.42	1.46	1.29	1.69	1.07	1.28	

Total of 4 ex-US PKAN pts currently being treated in accordance with local laws & regulations. 37

Source: Company Reports, Leerink Partners Research

While There Exists No Precedent of an Approved Drug in PKAN, RTRX May Learn from ApoPharma's Late-Stage Development in *Atypical* PKAN

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Product (sponsor)	Age of Onset	Title	Dosing	Upcoming Catalysts	Trial Identifier
Deferipron *(iron chelator)* ApoPharma	> 4 years	**Ph. 3 Trial of A Two-arm Efficacy and Safety Study of Deferiprone in Patients With Pantothenate Kinase-associated Neurodegeneration (PKAN)**	Dose will be escalated every 6 weeks starting at 5mg/kg, and increasing to 10mg/kg and finally 15 mg/kg) (oral solution BID)	Estimated primary completion date 05/2015	NCT01741532

- Primary Outcome Measures:
  - Changes in severity of dystonia – Barry-Albright Dystonia Scale (BADS) [6, 12, and 18 months]
  - Changes in patient's global impression of conditions improvement – Patient Global Impression of Improvement (PGI-I) [6, 12, and 18 months]

- Secondary Outcome Measures
  - Changes in globus pallidus iron levels – MRI T2* [18 months]
  - Changes in motor symptoms – Unified Parkinson's Disease Rating Scale (UPDRS) [6, 12, and 18 months]
  - Change in patient's quality of sleep – Pittsburgh Sleep Quality Index (PSQI) [6, 12 and 18 months]
  - Changes in measures of functional independence – WeeFIM or FIM [6, 12, and 18 months]
  - Safety and tolerability [18 months]

This IIT is partially funded by the European Commission's Seventh Framework Programme to the TIRCON consortium (Treat Iron-Related Childhood-Onset Neurodegeneration) and by the FDA OOPD (Dr. Elliott Vichinsky), highlighting the interest from regulators from both sides of the Atlantic to facilitate drug development in this debilitating disease

Source: Clinical trials.gov

Iron Chelators May Mechanistically Complement RE-024, Particularly in *Atypical* PKAN Symptomatically Worsening by Increased Iron Deposition

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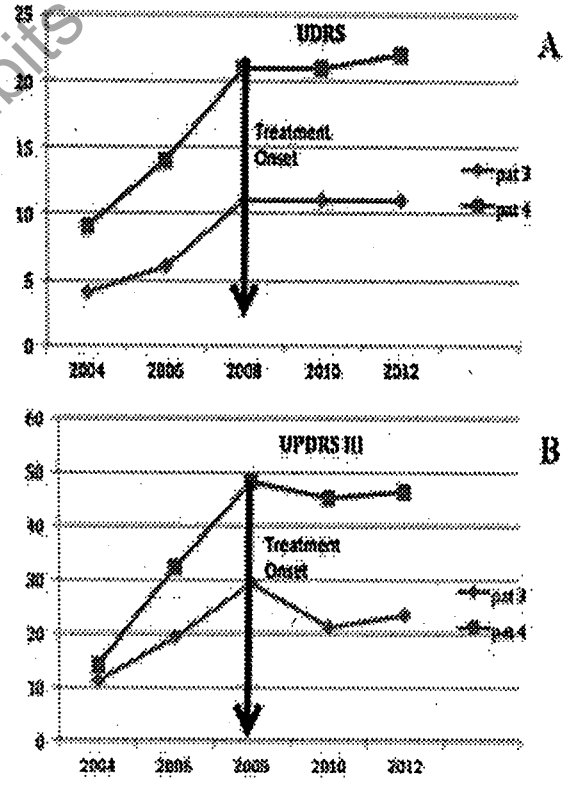
- In mid-stage trials, deferiprone has been studied with limited success based on the rationale that iron deposition in the basal ganglia is a hallmark of disease manifestation and progression

  - Efficacy: Ph. 2 results showed improvement in radiographic appearance (MRI) was noted; however, conclusive amelioration of symptoms was not observed
    - At 6 months follow-up, no change in clinical status in 10 patients, as assessed by the Burke-Fahn and Marsden Dystonia Rating Scales and a health-related quality of life scale
    - However, in the 4-year follow-up, 5/6 patients showed stabilization in motor symptoms (UPDRS and UDRS) that may suggest viability of long-term treatment in those less severely affected
  - Safety: mobilization of brain iron may lead to higher rate of complications with increased exposure of neural substrates to the metal's toxic effects, and thereby exacerbate the condition



Authors concluded a strong correlation of iron accumulation with age with the "adult-onset" subtype benefitting more from iron chelation treatment than the "childhood-onset" forms

Source: Zorzi et al., 2011; Cossu et al., 2014 ; Schipper, 2012

With IND Filing To Be Completed in 1H15, There Exists a Reasonable Upside to Our Launch Estimate of 2019 Given the Debilitating Nature of PKAN

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- In the total US prevalence of ~4,500 PKAN pts, we assume peak penetration of 33% in classic PKAN (75% of market) and 17% in atypical PKAN
- Both our 50% probability of success and $200,000 PPY are on the conservative side to account for uncertainty on the benefit of treatment and length of treatment duration
- We project a ~$130MM peak risk-adjusted market opportunity in 2028
- Several U.S. and foreign patents that constitute the patent family directed to RE-024 (and its analogs) in the treatment of PKAN expire in April 2033

RE-024 In PKAN Revenue Model	2014	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total PKAN pts in the US	4,500	4,500	4,500	4,500	4,500	4,500	4,500	4,500	4,500	4,500	4,500	4,500	4,500	4,500	4,500
Classic PKAN						75%	75%	75%	75%	75%	75%	75%	75%	75%	75%
Market Penetration (1st to market)						10%	16%	19%	22%	25%	28%	30%	31%	32%	33%
Atypical PKAN						25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
Market Penetration (2nd to market)						5%	8%	10%	11%	13%	14%	15%	16%	16%	17%
Total PKAN pts on Thiola	-	-	-	-	-	394	630	748	866	984	1,103	1,181	1,221	1,260	1,299
Annual Cost of Therapy						200,000	200,000	200,000	200,000	200,000	200,000	200,000	200,000	200,000	200,000
US Gross Revenues ($MM)						78.8	126.0	149.6	173.3	196.9	220.5	236.3	244.1	252.0	259.9
Probability of Success						50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
US Risk-Adjusted RE-024 Revenues ($MM)						39.4	63.0	74.8	86.6	98.4	110.3	118.1	122.1	126.0	129.9
Source: Company Reports, Leerink Partners Research															

Management and Upcoming Milestones

Management Team Has Previously Commercialized Several Orphan Disease Products, Notably at Biomarin and Genzyme

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Name	Title	Previous Work Experiences
Stephen Aselage	Chief Executive Officer (2012 - Present)	- Executive VP and Chief Business Officer, BioMarin (2005-12) - Sr VP Sales and Marketing, Cell Therapeutics (2004-05) - VP Sales and Marketing, Genzyme (1997-2003) - Director of Sales, Advanced Tissue Sciences (1995-97) - Director of Sales, Boehringer Mannheim (1993-94) - Director of Sales, Genentech (1986-93)
Horacio Plotkin	Chief Medical Officer (2013-Present)	- Executive Medical Director, Alexion (2010-13) - Medical Director, Genzyme (2007-10) MD from University of Buenos Aires School of Medicine
Maria Beconi	Chief Scientific Officer (2013-Present)	- Director, CHDI Foundation (2008-13) - Director, Abbott (2005-08) - Research Fellow, Merck (1999-04)
Alvin Shah, MD	Executive VP of R&D (2014-Present)	- Chief Operating Officer, Rare Disease Research Unit, Pfizer (2010-14) - Senior Engagement Manager, LEK Consulting (2006-10) - Resident Physician, Mass General Hospital (2003-06) MD from Alabama School of Medicine
Laura Clague, CPA	Sr. VP and Chief Finance Officer	- CFO of Amylin prior to acquisition by BMS (2003-14)

Source: Company Reports, Leerink Partners Research

Multiple Commercial and Pipeline Milestones Expected in the Next 6-18 Months

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	RTRX Catalysts	
Product	***Event***	***Timing***
Chenodal in cerebrotendinous xanthomatosis (CTX)	Ongoing discussions with FDA leading to a potential decision on including CTX in the label	YE15
Cholbam in Rare Bile Acid Disorders	Potential EU market entry	2016
Sparsentan in FSGS	Last patient enrolled in Ph. 2/3 study 8-week Primary Endpoint data (potentially registrational) Potential US Launch	YE2015 Mid-2016 2H2017
RE-024 in PKAN	US IND filing Initiation of Ph. 1 study Potential US launch	1H15 2015 2019
RE-034 in ACTH	US IND filing	2015

Source: Company Reports, Leerink Partners Research

P&L Model

Retrophin – P&L Model

Retrophin P&L ($MM)	1H14	3Q14	4Q14	2014	1Q15E	2Q15E	3Q15E	4Q15E	2015E	2016E	2017E	2018E	2019E	2020E
Product Revenues	**6.0**	**8.3**	**14.1**	**28.4**	**16.7**	**20.9**	**23.6**	**26.9**	**92.1**	**137.1**	**163.3**	**228.5**	**336.6**	**453.7**
Thiola in Cystinuria	4.00	4.76	8.84	17.60	10.88	12.24	13.60	14.96	51.68	78.88	95.20	108.80	122.40	136.00
Chenodal in CTX	2.00	3.59	5.24	10.83	5.10	5.74	6.39	7.64	24.88	33.91	36.75	39.69	42.75	45.93
Cholbam in Rare Bile Acid Disorders					0.74	2.97	3.62	4.29	15.50	24.34	31.35	40.41	52.43	68.80
Sparsentan in FSGS	-	-	-	-	-	-	-	-	-	-	-	39.60	79.59	139.98
RE-024 in PKAN		-	-	-	-	-	-	-	-	-	-	-	39.38	63.00
COGS	-	0.20	(0.83)	(0.64)	2.51	3.14	3.54	4.03	13.23	20.57	24.49	34.28	50.48	68.06
R&D	20.58	13.02	14.90	48.50	13.00	12.00	11.50	11.00	47.50	52.11	57.15	73.12	94.24	113.43
SG&A	22.60	18.58	18.72	59.90	15.00	15.50	16.00	17.00	63.50	65.82	70.22	86.83	117.79	145.19
Total Operating Expenses	43.19	31.79	32.78	107.76	30.51	30.64	31.04	32.03	124.23	138.50	151.87	194.23	262.51	326.67
Operating Loss	(37.19)	(23.44)	(18.70)	(79.33)	(13.78)	(9.69)	(7.43)	(5.14)	(32.17)	(1.37)	11.43	34.28	74.04	127.04
Interest Income	(2.18)	(2.63)	(2.63)	(7.43)	(2.63)	(2.63)	(2.63)	(2.63)	(7.88)	1.62	1.62	1.62	1.62	-
Finance Expense	(4.72)	(0.01)		(4.73)	(0.94)	(0.94)	(0.94)	(0.94)	(3.77)	(1.82)	(1.82)	(1.82)	(1.82)	-
Other Gains & Losses	(20.26)	6.53	(7.70)	(21.44)	-	-	-	-	-	-	-	-	-	-
EBT	(64.34)	(19.56)	(29.03)	(112.93)	(17.35)	(13.26)	(11.00)	(8.71)	(43.82)	(1.57)	11.23	34.07	73.84	127.04
Tax Expense (benefit)	2.46	-	-	2.46	-	-	-	-	-	-	-	-	-	-
Tax Rate												*36%*	*36%*	*36%*
Net Income (loss)	(61.88)	(19.56)	(29.03)	(110.47)	(17.35)	(13.26)	(11.00)	(8.71)	(43.82)	(1.57)	11.23	21.81	47.26	81.30
GAAP EPS	(2.46)	(0.73)	(1.10)	(4.29)	(0.51)	(0.39)	(0.32)	(0.26)	(0.97)	(0.04)	0.30	0.59	1.28	2.20
Diluted EPS	(2.68)	(0.89)	(1.10)	(4.68)	(0.50)	(0.39)	(0.32)	(0.25)	(0.96)	(0.04)	0.30	0.58	1.26	2.17
Basic Shares Outstanding	25.20	26.68	26.32	26.07	33.94	33.94	33.94	33.94	33.94	35.44	36.94	36.94	36.94	36.94
Diluted Shares Outstanding	25.20	28.21	26.32	26.58	34.45	34.45	34.45	34.45	34.45	35.95	37.45	37.45	37.45	37.45

Source: Company Reports, Leerink Partners LLC

RTRX BS & CFS ($MM) GAAP	1H14	3Q14	4Q14	2014	1Q15E	2Q15E	3Q15E	4Q15E	2015E	2016E	2017E	2018E	2019E	2020E
Net Cash	(67.9)	(62.4)	(66.2)	(66.2)	67.0	54.5	44.2	36.1	144.9	180.3	185.0	199.8	239.8	313.4
Cash & Equivalents	15.9	21.4	17.6	17.6	150.8	138.3	128.0	119.9	228.7	220.8	225.4	240.3	280.3	313.4
Debt	83.8	83.8	83.8	83.8	83.8	83.8	83.8	83.8	83.8	40.5	40.5	40.5	40.5	

Source: Company Reports, Leerink Partners Research

Disclosures Appendix

Analyst Certification

I, Joseph P. Schwartz, certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

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Distribution of Ratings/Investment Banking Services (IB) as of 12/31/14			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	150	70.00	60	40.00
HOLD [MP]	64	30.00	1	2.00
SELL [UP]	0	0.00	0	0.00

Explanation of Ratings

Outperform (Buy): We expect this stock to outperform its benchmark over the next 12 months.
Market Perform (Hold/Neutral): We expect this stock to perform in line with its benchmark over the next 12 months.
Underperform (Sell): We expect this stock to underperform its benchmark over the next 12 months.The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.
For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than $2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over $2 billion.

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New York

Boston

San Francisco

From: Michael Smith
To: Nancy Retzlaff; Tina Ghorban
Sent: 4/29/2015 4:03:27 PM
Subject: RE: Sulfadiazine

A few updates:

Discussions are progressing w/ Sandoz and they want to hear more about our capabilities. They want a commercial deck, focused on our ability to provide things that they can't. We've cited our ability to build commercial teams around underserved pt populations which seems to resonate well with them. The commercial deck should highlight our ability to grow TRx and improve patient services.

We are also now in the process of bidding for Daraprim (pyrimethamine), a sole source product from Impax Labs. Pyrimethamine + sulfadiazine combo therapy is the gold standard for toxoplamosis. I would build a similar deck specific to daraprim.

The sooner you can turn this around the better. We're speaking w/ Impax tomorrow. In tandem, we think these products could do >500mm annually. I'm free to discuss whenever.

From: Michael Smith
Sent: Friday, April 24, 2015 3:26 PM
To: Nancy Retzlaff; Tina Ghorban
Subject: Sulfadiazine

Another item to keep on your radar is Sulfadiazine. It is a sole-source (US only, generic ex-us) infectious disease product from Sandoz, indicated for toxoplasmosis. This would be the classic closed distribution play - we think it could do >250mm per annum. I've attached a short deck and the model for some quick background.

Michael Smith
Senior Director
Business Development

Turing Pharmaceuticals

[redacted]

DRAFT

TURING
PHARMACEUTICALS

Commercial Capabilities

May 2015

[redacted]

Experienced and Fast-Growing Commercial Team

Executive	Experience
Nancy Retzlaff *Chief Commercial Officer*	• More than 20 years of biopharmaceutical commercial leadership experience including sales, marketing, commercial development & business leadership roles at Bayer, Schering-Plough, Pfizer & Mesoblast
Richard DeYoung *Head of Sales & National Accounts*	• More than 15 years of biopharmaceutical experience leading sales, key accounts and managed markets teams at Takeda and Astra Zeneca
Tina Ghorban *Senior Director, Business Analytics & Customer Insights*	• 15 years of biopharmaceutical experience in market analytics, global commercial development, new product marketing and US marketing at Pfizer, Shionogi and Mesoblast
Scott Emmens *Sales Director: Vecamyl*	• 15 year biopharmaceutical sales leadership experience including sales operations and sales training at Astra Zeneca, Takeda and Shire

<u>Relevant Experience and Skill Sets:</u>

- Therapeutic areas expertise include orphan & rare disease (HIV, oncology, ?) and broader disease areas (pain, IBD, anemia, diabetes, cardiovascular, respiratory, endocrinology, CNS)
- Experience across broad range of product lifecycles, including global and US launches, mature brands, peri-LOE and branded generics
- Creation of complete commercial organization and infrastructure, as well as leading organizations through dynamic change and growth
- Alignment of marketing & sales around a specialty distribution strategy and patient services platform
- Creation of strategic brand platform, market development plan, and communication platforms. Tactical execution of all planned activities.
- Strategic planning and execution with all key customers, including KOLs, physicians, payers, patients and patient advocacy

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Turing Organizational Strengths

- Ability to build commercial teams around underserved patient populations

- Nimble, able to scale-up quickly and efficiently
  - Built sales and MSL customer-facing organization and commercial operations infrastructure within 3 months

- Experience with specialty, closed distribution model

Daraprim (pyrimethamine) Commercial Overview

- **Component of gold standard therapy for treatment of toxoplasmosis**
  - Combination with Pyrimethamine + Sulfadiazine + Leucovorin is considered gold standard with proven efficacy
- **Small "at-risk" patient population**
  - While 30% of US population is seropositive for toxoplasmosis, only immunocompromised patients are at risk for developing symptoms and complications from infection
  - HIV patients represent ~90% of total patients treated with Daraprim, and 80% of the sales.
  - Congenital toxoplasmosis accounts for 10% patients but over 20% of sales due to a longer treatment regimen.
- **Near term revenue generation potential**
  - 2014 US revenue of $9.6M

AIDSMEDS
Your Ultimate Guide to HIV Care

	2011	2012	2013	2014
TRx	12,772	11,604	9,905	8,821
Sales	$6.079	$7.884	$8.681	$9.598

THE PAGE (OR PAGES) OMITTED FROM THIS DOCUMENT ARE UNDER SEAL

Plans for Future Growth

- **Price Increase**
  - Current pricing lower than other adjunctive therapies, so could increase price immediately
  - Physician community less sensitive to price increases, but need to determine the price point at which payers start to increase cost-sharing with patients, which could result in physician switching
- **Commercial Expansion**
  - Partner with patient advocacy organization to support Direct-to-Patient campaign to raise awareness, speed diagnosis and treatment rates of toxoplasmosis
  - Partner with HIV community and ACOG to treat prophylactically for toxo?
    - Potential neurological damage creating psychological symptoms?
- **Lifecycle Strategy**
  - Explore fixed-dose combination to improve adherence and ease of use
  - Additional indications?

Daraprim (pyrimethamine) Challenges

- **How interchangeable are treatments for toxoplasmosis? Does it vary by severity of infection, by patient type, or any other factors?**
  - Possible competitors: Atovaquone, Bactrim (trimethoprim-sulfamethoxazole), clindamycin, dapsone (for sulfa)
  - Dedicoat M, Livesley N: Management of toxoplasmic encephalitis in HIV-infected adults (with an emphasis on resource-poor settings). *Cochrane Database Syst. Rev.* 19(3), CD005420 (2006)
    - Three trials were found to meet the inclusion criteria for this review. Two trials compared pyrimethamine plus sulfadiazine (P+S) with pyrimethamine plus clindamycin (P+C). One trial compared P+S with trimethoprim-sulfamethoxazole (TMP-SMX). Conclusions were that the available evidence fails to identify any one superior regimen for the treatment of TE. The choice of therapy will often be directed by available therapy. Given the current evidence, TMP-SMX appears to be an effective alternative therapy for TE in resource-poor settings where P+S are not available.
  - Randomized Phase II Trial of Atovaquone with Pyrimethamine or Sulfadiazine for Treatment of Toxoplasmic Encephalitis in Patients with Acquired Immunodeficiency Syndrome: ACTG 237/ANRS 039 Study. Keith Chirgwin, et al. Clinical Infectious Diseases 2002; 34:1243–50
  - The combination of pyrimethamine plus clindamycin is as effective as pyrimethamine plus sulfadiazine during the acute phase of therapy. Rash and diarrhea are common adverse effects of pyrimethamine plus clindamycin. A randomized, prospective study reported that trimethoprim-sulfamethoxazole (Bactrim) is as effective as pyrimethamine plus sulfadiazine for the treatment of *toxoplasmic encephalitis.*
  - Bactrim most commonly used to prevent toxo in patients with <100 CD4's

- **What is the cost sensitivity to combination therapy treatment? What price or scenario would trigger a physician to prescribe another product combination rather than the gold standard of pyrimethamine + sulfadiazine + leucovorin?**
  - Total cost of treatment needs to be considered when raising price
    - Total cost of therapy is >$2.5k for HIV patients and >$6,500 for congenital toxo.
  - HIV patient advocacy may react to price increase
    - HIV community is highly organized, sensitive, and action-oriented
    - Significant price increases that disproportionately affect this community could result in backlash from patient advocacy groups, particularly if payers increase cost sharing with patients

- **How stable is the flow of toxoplasmosis patients?**
  - Fewer HIV patients becoming immunocompromised with better combination therapy
    - Seroprevalence of anti-*Toxoplasma* antibody varies substantially among different geographic locales, with a prevalence of approximately 11% in the United States, versus 50% to 80% in certain European, Latin American, and African countries. In the era before antiretroviral therapy (ART), the 12-month incidence of TE was approximately 33% in patients with advanced immunosuppression who were seropositive for *T. gondii* and not receiving prophylaxis with drugs against the disease. A low incidence of toxoplasmosis is seen in patients who are seronegative for *T. gondii*. -- Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents, Recommendations from the Centers for Disease Control, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America
  - Daraprim (pyrimethamine) Rx's down on average 10% for last four years

Appendix

TURING
PHARMACEUTICALS

[redacted]

Toxoplasmosis Clinical Presentation

Immunocompromised Patients

- Initially presents with non-specific symptoms such as headache, lethargy, and fever
- If untreated, disease can progress to focal encephalitis, ataxia, loss of memory, dementia, speech abnormalities, hemiparesis, seizures, and coma
- Primary lesions of cerebral necrosis, but retinal lesions are common if the infection disseminates to the eye

Congenital Toxoplasmosis

- Risk of infection increases with each trimester, but infections in the first trimester lead to the most severe disease
- Congenital infection can lead to a wide variety of manifestations including spontaneous abortion, hydrocephalus or microcephalus, CNS calcification, retinochorioditis, and failure to thrive
- Some symptoms that can present later in infancy and childhood include learning disabilities, growth retardation, mental retardation, convulsions, palsies, blindness and deafness

BD-Financial Projections

- **Toxoplasmosis is a rare disease and should be priced appropriately**
  - $50,000+ is the target price for Sulfadiazine
    - Current Hepatitis C cost for cure > $100,000
    - Net present value of HIV treatment > $250,000
    - Both significantly more prevalent and have multiple treatment options

- **With repricing, revenues may exceed $200 million**
  - Turing plans a step-wise price increase which will allow management to "course correct" if unforeseen challenges arise
  - Even at a modest PPPY of $10,000, revenues of $50 million are possible, representing substantial upside

- Turing management has experience with significant price increases while at Retrophin

From: Michael Smith
To: Edwin Urrutia
Sent: 5/5/2015 6:04:36 PM
Subject: FW: Daraprim
Attachments: Commercial Capabilities for BD.pptx

I would change a lot of this, but not a bad start

From: Tina Ghorban
Sent: Tuesday, May 5, 2015 4:37 PM
To: Michael Smith
Cc: Nancy Retzlaff
Subject: Daraprim

Hi Mike,

Here's a DRAFT deck that includes Commercial capabilities (just a few slides), our thoughts on the commercial opportunity of Daraprim and some possible challenges (which we obviously wouldn't present with the commercial capabilities). The challenges (listed below) may or may not warrant further exploration given your prior discussions with KOL's. Let's chat when you have a chance.

Daraprim Challenges
• How interchangeable are treatments for toxoplasmosis? Does it vary by severity of infection, by patient type, or any other factors?
- Possible competitors: Atovaquone, Bactrim (trimethoprim-sulfamethoxazole), clindamycin, dapsone (for sulfa)
- Dedicoat M, Livesley N: Management of toxoplasmic encephalitis in HIV-infected adults (with an emphasis on resource-poor settings). Cochrane Database Syst. Rev. 19(3), CD005420 (2006)
§ Three trials were found to meet the inclusion criteria for this review. Two trials compared pyrimethamine plus sulfadiazine (P+S) with pyrimethamine plus clindamycin (P+C). One trial compared P+S with trimethoprim-sulfamethoxazole (TMP-SMX). Conclusions were that the available evidence fails to identify any one superior regimen for the treatment of TE. The choice of therapy will often be directed by available therapy. Given the current evidence, TMP-SMX appears to be an effective alternative therapy for TE in resource-poor settings where P+S are not available.
- Randomized Phase II Trial of Atovaquone with Pyrimethamine or Sulfadiazine for Treatment of Toxoplasmic Encephalitis in Patients with Acquired Immunodeficiency Syndrome: ACTG 237/ANRS 039 Study. Keith Chirgwin, et al. Clinical Infectious Diseases 2002; 34:1243-50
- The combination of pyrimethamine plus clindamycin is as effective as pyrimethamine plus sulfadiazine during the acute phase of therapy. Rash and diarrhea are common adverse effects of pyrimethamine plus clindamycin. A randomized, prospective study reported that trimethoprim-sulfamethoxazole (Bactrim) is as effective as pyrimethamine plus sulfadiazine for the treatment of toxoplasmic encephalitis.
- Bactrim most commonly used to prevent toxo in patients with <100 CD4's
• What is the cost sensitivity to combination therapy treatment? What price or scenario would trigger a physician to prescribe another product combination rather than the gold standard of pyrimethamine + sulfadiazine + leucovorin?
- Total cost of treatment needs to be considered when raising price
§ Total cost of therapy is >$2.5k for HIV patients and >$6,500 for congenital toxo.
- HIV patient advocacy may react to price increase
§ HIV community is highly organized, sensitive, and action-oriented
§ Significant price increases that disproportionately affect this community could result in backlash from patient advocacy groups, particularly if payers increase cost sharing with patients
• How stable is the flow of toxoplasmosis patients?
- Fewer HIV patients becoming immunocompromised with better combination therapy
§ Seroprevalence of anti-Toxoplasma antibody varies substantially among different geographic locales, with a prevalence of approximately 11% in the United States, versus 50% to 80% in certain European, Latin American, and African countries. In the era before antiretroviral herapy (ART), the 12-month incidence of TE was approximately 33% in patients with advanced mmunosuppression who were seropositive for T. gondii and not receiving prophylaxis with drugs against the disease. A low incidence of toxoplasmosis is seen in patients who are seronegative for T. gondii. -- Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents, Recommendations from the Centers for Disease Control, the

National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America
- Daraprim (pyrimethamine) Rx's down on average 10% for last four years

'ina Ghorban
Senior Director
Business Analytics & Customer Insights

Turing Pharmaceuticals
[redacted]

From: Michael Smith
To: Martin Shkreli
Sent: 5/23/2015 8:17:33 PM
Subject: RE: Generic Launch Analysis
Attachments: 5-15mm Gx Evaluation.xlsx

Attached

From: Martin Shkreli
Sent: Saturday, May 23, 2015 6:28 PM
To: Michael Smith
Subject: RE: Generic Launch Analysis

Can I get the list?

From: Michael Smith
Sent: Friday, May 22, 2015 11:47 AM
To: Martin Shkreli
Subject: RE: Generic Launch Analysis

Excluding any on patent currently:

5-15mm: 11 branded, 3 went generic (27%)
1-15mm: 44 branded, 11 went generic (25%)

Need to find a source for historical LOE in for orange book patents. I've now reviewed each one of these drugs, so I'm confident that these numbers are accurate for this sample.

From: Martin Shkreli
Sent: Friday, May 22, 2015 10:53 AM
To: Michael Smith
Subject: RE: Generic Launch Analysis

We should exclude any on patent

From: Michael Smith
Sent: Friday, May 22, 2015 10:51 AM
To: Martin Shkreli
Subject: RE: Generic Launch Analysis

5-15mm: 16 branded, 6 went generic (37.5%)
1-15mm: 49 branded, 12 went generic (24.5%)

From: Martin Shkreli
Sent: Friday, May 22, 2015 10:26 AM
To: Michael Smith
Subject: RE: Generic Launch Analysis

Hmmmm interesting

From: Michael Smith
Sent: Friday, May 22, 2015 10:25 AM
To: Martin Shkreli
Cc: Edwin Urrutia; Patrick Crutcher; Chris Lau
Subject: RE: Generic Launch Analysis

12 branded products with 5-10mm in 2010, 5 went generic by Q115 (42%)
44 branded products with 1-10mm in 2010, 11 went generic by Q115 (25%)

From: Martin Shkreli
Sent: Thursday, May 21, 2015 10:54 PM
To: Michael Smith
Subject: RE: Generic Launch Analysis

The question on 50mm is less is not what % were between 5-10m
The question is for drugs between 5-10m how many went generic?

From: Michael Smith
Sent: Thursday, May 21, 2015 10:37 PM
To: Martin Shkreli
Cc: Patrick Crutcher; Edwin Urrutia; Chris Lau
Subject: Generic Launch Analysis

I've attached an interim analysis of the generic launch screen, evaluating the innovator's sales and units in the years prior to a generic launch. This interim analysis covers 680 molecules and 5438 products. We are currently working on more extensive version covering everything on IMS.

50mm or less

- For products with less than $50mm in sales that were genericized between 2009-2014 (n=14), 36% (5) had between 5-10mm in sales and 21%(3) had between 0-5mm in sales 3 years prior to generic launch

- 3 years prior to gx launch, average sales for the sub-50 group were 15.7 (median 8.3) and average units were 67k (median 57k)
Low Units (<100K)

- For products with less than 100k units (n=13), 23% (3) had sales more than 10mm, 38% (5) had sales between 5-10mm and 38% (5) had sales 0-5mm 3 years prior to generic launch

- 3 years prior to gx launch, average sales for the Low Units group were 26.7 (median 6.5) and average units were 51.9k (median 31.1k)

- 3 years prior to gx launch, 3 drugs had between 0-10k units and 1 had between 10-20k units.
"Any Size" group

- For all products genericized (n=74), 30% (22) had sales between 0-50mm, 46% (34) had between 50-500mm and 24% (18) had more than 500mm 3 years prior to genericization

- 3 years prior to launch, average sales for the "any size" group were 511mm (median 147mm) and average units were 2.0mm (median 336k)

It appears as though sub 50mm products are the most frequently genericized. This may be due to the fact that there are probably more drugs floating around in the 0-100 range than one might think. At first blush, it seems like the smallest products (~5mm) usually get genericized by small companies. I think the most important take away is that 10.8% (8/74) of drugs had revs 0-10mm 3 years prior to generic launch and only 5% of drugs (4/74) had less than 20k units.

Chris and I will keep working on the complete one.

Michael Smith
Senior Director
Business Development

Turing Pharmaceuticals
[redacted]

TURING

PHARMACEUTICALS

Project Dart

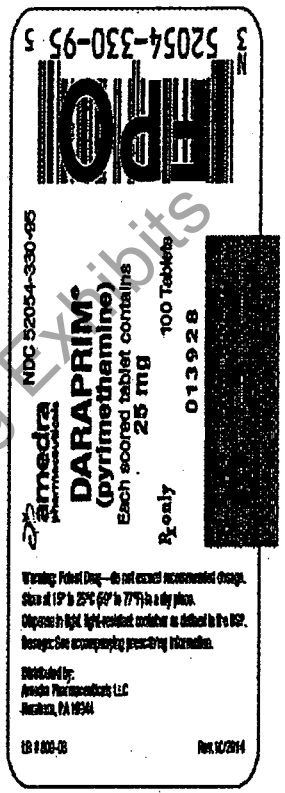
June 2015

Executive Summary

- **Proposed term sheet to acquire/license Daraprim® (pyrimethamine) from Impax Labs (IPXL)**
  - Turing offered 6x 2014 US net sales (~$45mm)
  - 2014 US gross revenue of ~$10mm
- **Daraprim® is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide, since synergism exists with this combination.**
  - FDA approved in January 1953 (NDA #008578)
  - Gold standard of care for toxoplasmosis
- **We believe there are several potential strategies to grow revenue**
  - Current pricing lower than other adjunctive therapies
  - Daraprim® fits the specialty distribution business model

Daraprim Prescribing Information and Pricing

- **Daraprim® is indicated for the treatment of toxoplasmosis encephalitis**
  - Approved January 23, 1953
  - No approved generics or recent DMFs
- **Current gold standard for Toxoplasmosis**
  - Coadministered with sulfadiazine
  - Inhibits DHFR, disrupting folate synthesis
- **Dose: 50–75mg/day**
  - 25mg, 100 count bottle
  - ~$3,000 PPPY
- **Payor Mix**
  - 45% Commercial
  - 25% Medicaid
  - 25% Medicare Part D
  - 5% Cash



	2011	2012	2013	2014	2015(April)
TRx	12,772	11,604	9,905	8,821	2,626
Gross Sales ($mm)	$6.273	$8.163	$8.938	$9.932	$3.004

Toxoplasmosis Overview

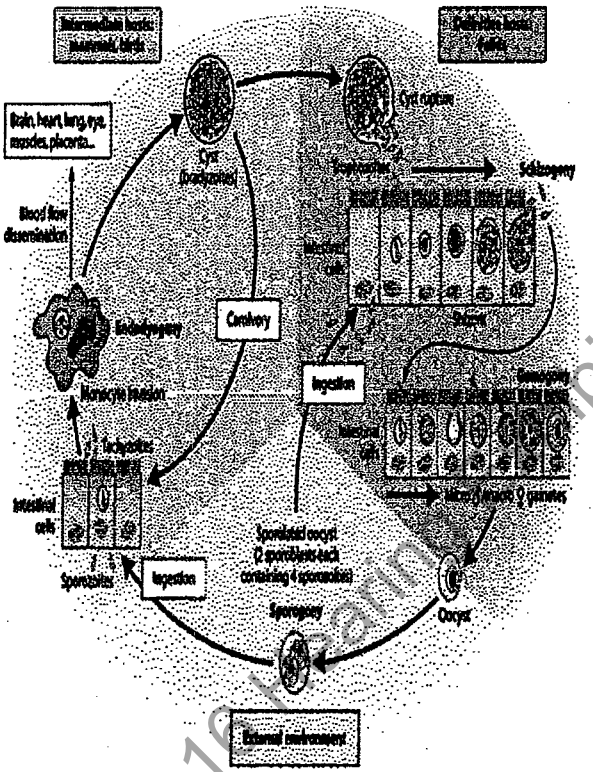


FIG 2 Life cycle of Toxoplasma gondii. Shown are the biology, infection, and replication of the three infective stages of the parasites in their respective hosts.

- Approximately 15% of US population is seropositive for toxoplasmosis (30% worldwide, >50% in Brazil)
- Patients become infected by ingesting cysts in undercooked pork or oocysts in contaminated water
- Toxoplasmosis can cause severe neurological, ocular, and systemic diseases in neonates and individuals with weakened immune systems
- Symptoms self-resolve in immunocompetent hosts, though cysts containing dormant bradyzoites will remain throughout life, predominantly in the brain, CNS and musculature

<u>Toxoplasmosis is always life threatening for neonates and the immunocompromised</u>

Toxoplasmosis Clinical Presentation

Immunocompromised Patients

- Majority of patients are HIV positive with CD4+ counts < 100
  - Occasional incidence in immunosuppressed transplant patients
- Initially presents with non-specific symptoms such as headache, lethargy, and fever
- Disease is usually identified when patients present with difficulty walking, weakness on one side of the body (hemiparesis), seizure, speech abnormalities and loss of memory
- If untreated, further cerebral necrosis leads to dementia, status epilepticus, coma and death
- Primary lesions of cerebral necrosis, but retinal lesions are common if the infection disseminates to the eye, which can lead to blindness

Congenital Toxoplasmosis

- Estimated incidence of 1:10,000 births
- Risk of infection increases with each trimester, but infections in the first trimester lead to the most severe disease
- Congenital infection can lead to a wide variety of manifestations including spontaneous abortion, hydrocephalus or microcephalus, CNS calcification, retinochorioditis, and failure to thrive
- Symptoms that present later in infancy and childhood include learning disabilities, growth retardation, mental retardation, convulsions, palsies, blindness and deafness

New Entrant Feasibility

- **Under GDUFA, ANDAs filed on or after October 1, 2012 referencing Type II DMFs must use a DMF listed on the "Available for Reference" list to avoid receiving a "Refuse to Receive" response from FDA**
  - ANDAs may instead include their own CMC package, though recent FDA guidance suggest this is not preferred and few recent examples suggest it very uncommon
- **There are only two Active DMF filers for pyrimethamine**
  - 11/26/1992 Fukuzyu Pharmaceutical (Japan)
  - 6/26/2009 IPCA Laboratories (India)
- **Though both DMF filers are considered "Active", only IPCA is listed as "Available for Reference"**
  - Two Requirements for "Available for Reference":
    - GDUFA DMF fee (IPCA paid 8/22/2013)
    - Completeness assessment (IPCA completed 11/27/2013)
- **Turing believes an ANDA was likely filed in 2014 using IPCA's API**
  - FDA released bioequivalence guidance for pyrimethamine in March 2015, likely in response to an earlier filing
  - Fukuzyu currently in an exclusive supply agreement (Impax) and not listed as "Available for Reference"
- **IPCA has had substantial manufacturing issues that will significantly disrupt any filing in process**

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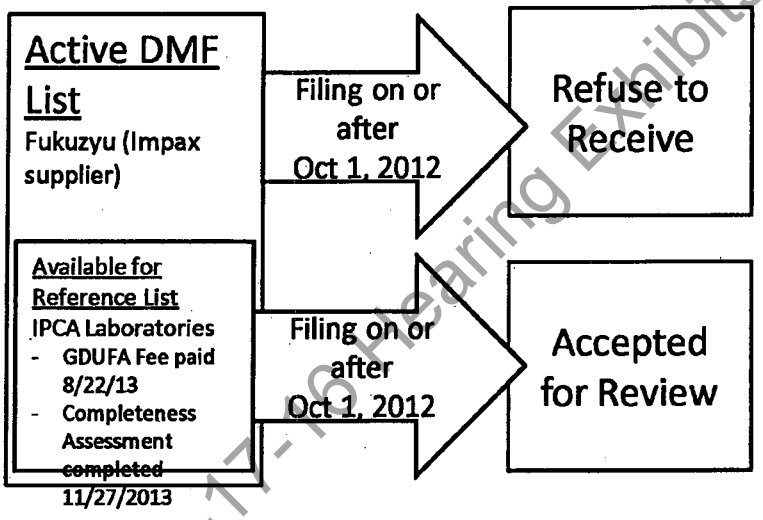

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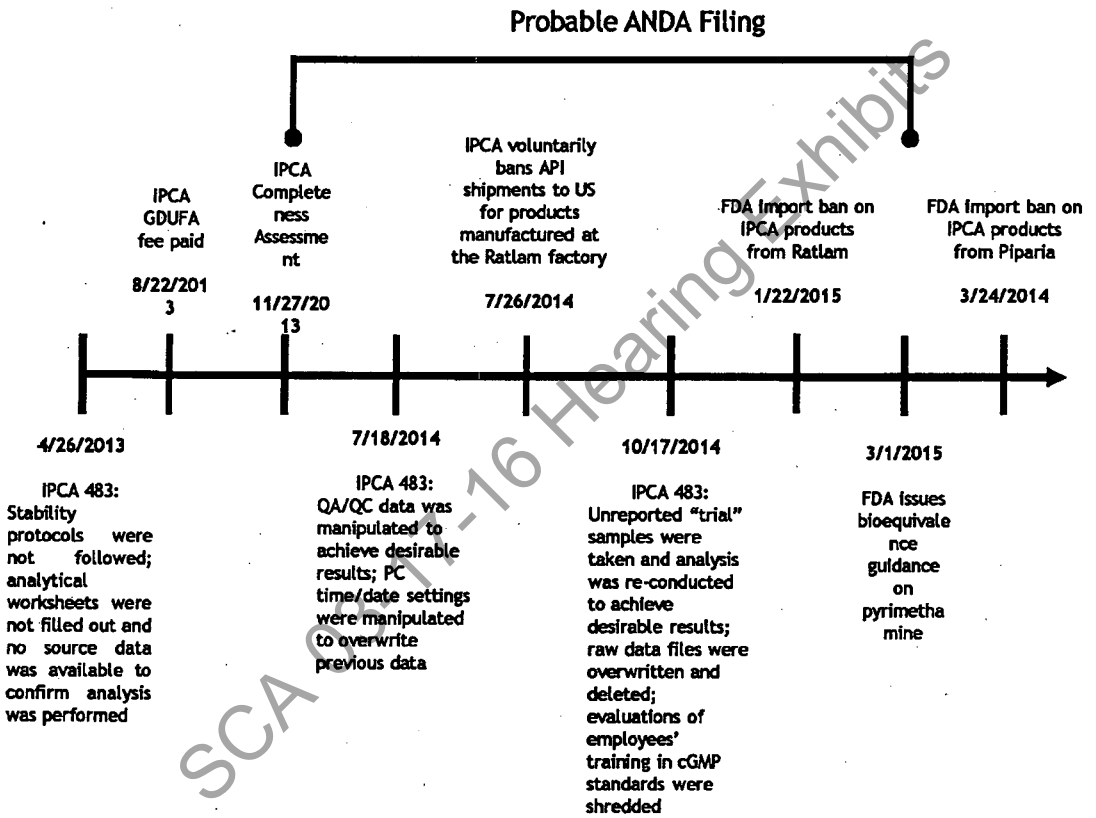

New Entrant Feasibility

- **Potential filer may stay with IPCA**
  - IPCA has confirmed that they will unable to supply pyrimethamine for at least 12 months
  - Citizens petition could further delay any ANDAs filed with IPCA supply
- **Potential filer may have moved to a new vendor**
  - Additional 6 months minimum for long term and accelerated stability
  - Appearance in the "Available for Reference" list will validate this theory
  - Major amendment to ANDA will push approval date back 1-2 years
- **Turing believes Daraprim will remain sole source until at least mid 2016**
- **If no developments have occurred by 2016, Turing believes Daraprim could remain sole source much longer**

Lifecycle Management

- **Line extensions**
  - Once-a-day pill
  - Combination with sulfadiazine
- **Next generation analogues**
  - No new medicines have been approved in >40 years
  - Improved potency, avoid teratogenicity
  - Target T. gondii DHFR
    - Pyrimethamine more active against human DHFR
- **Toxoplasmosis Vaccine**
  - Academics have made progress in several vaccines targeting various surface antigens
    - SAG1

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Experienced and Fast-Growing Commercial Team

Executive	Experience
Nancy Retzlaff *Chief Commercial Officer*	• More than 20 years of biopharmaceutical commercial leadership experience including sales, marketing, commercial development & business leadership roles at Bayer, Schering-Plough, Pfizer & Mesoblast
Richard DeYoung *Head of Sales & National Accounts*	• More than 15 years of biopharmaceutical experience leading sales, key accounts and managed markets teams at Takeda and Astra Zeneca
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Scott Emmens *Sales Director*	• 15 year biopharmaceutical sales leadership experience including sales operations and sales training at Astra Zeneca, Takeda and Shire

Relevant Experience and Skill Sets:

- Therapeutic areas of expertise include orphan & rare diseases and specialty areas (HIV, pain, oncology, neuroscience, cardiovascular, respiratory, endocrinology, CNS)
- Experience across broad range of product lifecycles, including global and US launches, mature brands, pre-LOE and branded generics
- Creation of complete commercial organization and infrastructure, as well as leading organizations through dynamic change and growth
- Alignment of marketing & sales around specialty distribution strategy and patient services platform
- Creation of strategic brand platform, market development plan, and communication platforms. Tactical execution of all planned activities.
- Strategic planning and execution with all key customers, including KOLs, physicians, payers, patients and patient advocacy

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Financial Projections

- **Toxoplasmosis is a rare disease and should be priced appropriately**
  - Current Hepatitis C cost for cure > $100,000
  - Net present value of HIV treatment > $250,000
  - Both significantly more prevalent and have multiple treatment options
- **Turing management has experience with similar revenue growth strategies while at Retrophin**
  - Specialty sales force
  - High-touch closed distribution system
  - Improved patient advocacy and support
- **Potential revenues of over $500mm with greater than 80% EBITDA margins**
- **Turing plans to finance the transaction with a combination of debt and equity**

TURING
PHARMACEUTICALS

Project Dart

June 2015

TURING

PHARMACEUTICALS

Project Dart

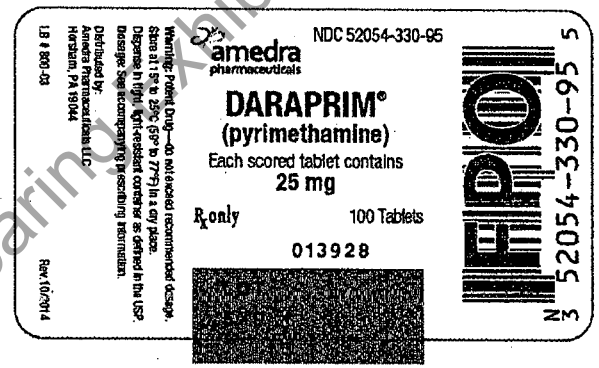
June 2015

Executive Summary

- **Turing is in discussions to acquire Daraprim® (pyrimethamine) from Impax Labs (IPXL)**
  - 2014 US net revenue of $4.9mm
  - Initial offer of 6x 2014 US net sales ($29.5mm)
- **Daraprim® is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide, since synergism exists with this combination**
  - FDA approved in January 1953 (NDA #008578)
  - Gold standard of care for toxoplasmosis
- **Turing is looking to borrow $5mm – $15mm in senior secured debt**
  - The transaction will be financed with a combination of debt and equity
- **We believe there are several potential strategies to grow revenue**
  - Current pricing lower than other adjunctive therapies
  - Daraprim® fits the specialty distribution business model

Daraprim Prescribing Information and Pricing

- **Daraprim® is indicated for the treatment of toxoplasmosis encephalitis**
  - Approved January 23, 1953
  - No approved generics or recent DMFs
- **Current gold standard for Toxoplasmosis**
  - Co-administered with sulfadiazine
  - Inhibits DHFR, disrupting folate synthesis
- **Dose: 50 – 75mg/day**
  - 25mg, 100 count bottle
  - ~$3,000 PPPY
- **Payor Mix**
  - 45% Commercial
  - 25% Medicaid
  - 25% Medicare Part D
  - 5% Cash



Actual	2011	2012	2013	2014	Q1:2015
Units (bottles)	12,600	11,004	10,260	9,708	1,836
Net Sales (mm)	$5.114	$5.620	$5.829	$4.932	$1.226

Gross-to-Net Calculation

- **Chargebacks may be specific to Impax's current contracts with group purchasing organizations (GPOs) and managed care**
  - Current pyrimethamine chargeback terms likely a result of negotiated terms for a larger Impax portfolio

	2011	2012	2013	2014	Q1:15
Gross Revenue	9,138,946	10,650,678	12,067,428	13,146,270	2,488,661
Cash Discount	182,779	213,014	241,348	256,317	51,003
Medicaid	1,104,817	1,812,187	2,878,267	3,348,557	699,472
Returns	673,025	532,534	241,176	1,061,405	(72,997)
Rebates	612,949	746,747	683,141	864,634	183,242
Discount Rebate	-	-	10,056	9,765	2,290
Chargebacks	1,450,864	1,725,553	2,183,854	2,673,073	398,986
Net Revenue	**5,114,512**	**5,620,644**	**5,829,586**	**4,932,521**	**1,226,665**
Units	12,576	11,004	10,260	9,708	1,836
Px/unit	727	968	1,176	1,354	1,355
Realized Px/unit	407	511	568	508	668
Cash Disc	2.0%	2.0%	2.0%	1.9%	2.0%
Medicaid	12.1%	17.0%	23.9%	25.5%	28.1%
Returns	7.4%	5.0%	2.0%	8.1%	-2.9%
Rebates	6.7%	7.0%	5.7%	6.6%	7.4%
Dis Rebate	0.0%	0.0%	0.1%	0.1%	0.1%
Chargebacks	15.9%	16.2%	18.1%	20.3%	16.0%
Net Revenue	56.0%	52.8%	48.3%	37.5%	49.3%

Toxoplasmosis Overview

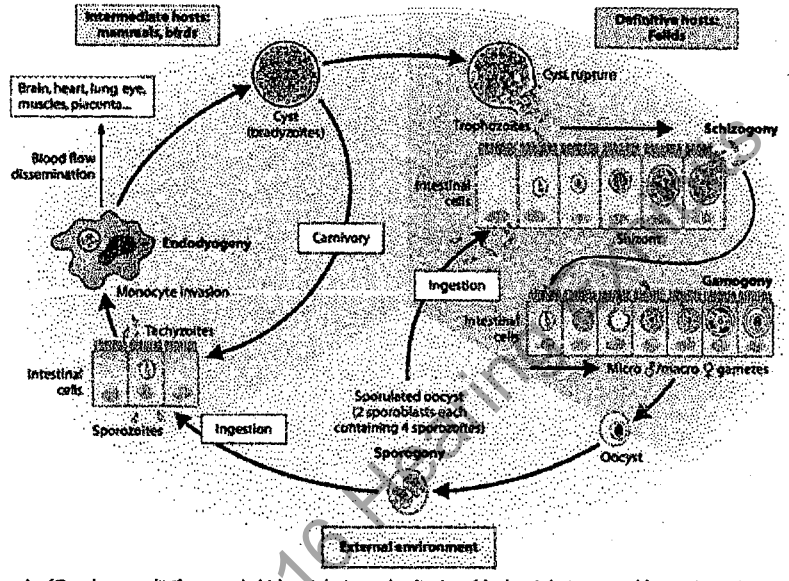


FIG 2 Life cycle of *Toxoplasma gondii*. Shown are the biology, infection, and replication of the three infective stages of the parasites in their respective hosts.

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Toxoplasmosis Clinical Presentation

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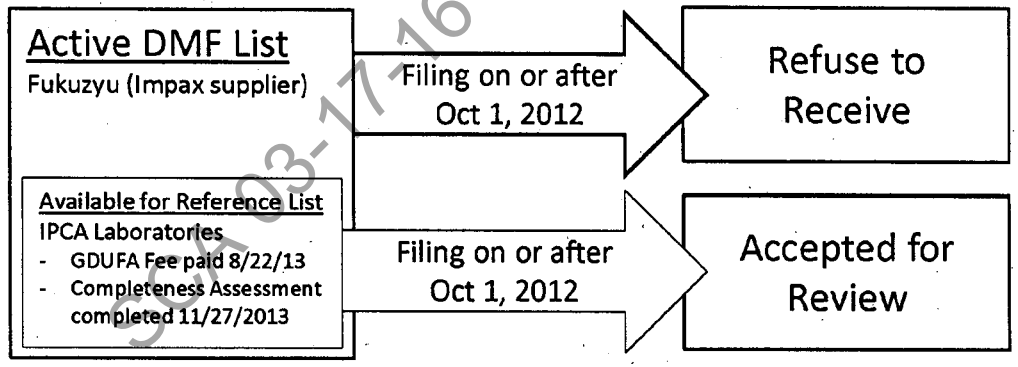

New Entrant Feasibility

- **Data Integrity is a very important issue for FDA**
  - IPCA will have to conduct very rigorous review of data reporting standards
  - Any ANDAs currently on file will likely be put on hold
- **Potential filer may stay with IPCA**
  - IPCA has confirmed that they will be unable to supply pyrimethamine for at least 12 months
    - Independent consultants believe this timeline is "very aggressive"
  - Citizens petition could further delay any ANDAs filed with IPCA supply
  - There is no protocol for lifting import bans, which may delay process further
- **Potential filer may have moved to a new vendor**
  - Appearance in the "Available for Reference" list will signal the refiling/amendment
  - Filer will need to requalify any API and re-validate processes and methods
  - Additional 6 months minimum for long term and accelerated stability
  - Major amendment to ANDA will further delay review date
  - FDA may allow filing without additional bioequivalence
- **Turing believes Daraprim will remain sole source until at least mid 2016**
- **If no developments have occurred by 2016, Turing believes Daraprim could remain a single source product much longer**

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- **Line extensions**
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  - Combination with sulfadiazine
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  - Improved potency, avoid teratogenicity
  - Target T. gondii DHFR
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  - Improved patient advocacy and support
- **Potential revenues of over $500mm with greater than 80% EBITDA margins**
- **Turing plans to finance the transaction with a combination of debt and equity**

Financial Model

- **Illustrative Model**
  - Assumes $200,000 per unit

	2011	2012	2013	2014	Partial 2015	Full 2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Net Revenue (mm)	5.1	5.6	5.8	4.9	336.5	339.2	854.7	880.4	90.7	9.3	1.0	1.0	1.0	1.1	1.1	1.1
Total COGS	0.6	0.5	3.6	0.4	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Gross Profit	4.5	5.1	2.2	4.6	333.5	336.2	851.7	877.4	87.7	6.3	-2.0	-2.0	-2.0	-1.9	-1.9	-1.9
R&D	0.0	0.0	0.0	0.0	4.0	4.0	4.0	4.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sales Force	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FTE Salary	0.0	0.0	0.0	0.0	0.264	0.270	0.276	0.282	0.288	0.294	0.300	0.306	0.312	0.318	0.325	0.331
Sales & Marketing	0.0	0.0	0.0	0.0	3.8	3.8	7.6	7.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
G&A	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OPEX	1.0	1.0	1.0	1.0	8.8	8.8	12.6	12.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Operating Income	**3.5**	**4.1**	**1.2**	**3.5**	**324.8**	**327.4**	**839.1**	**864.7**	**87.7**	**6.3**	**-2.0**	**-2.0**	**-2.0**	**-1.9**	**-1.9**	**-1.9**
Interest Expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest Income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	21.3	37.9	40.3	41.2	41.9	42.7	43.4	44.2	45.0
Pre-tax Income	3.5	4.1	1.2	3.5	324.8	327.4	839.1	886.0	125.6	46.6	39.1	39.9	40.7	41.5	42.3	43.1
Taxes	0.2	0.2	0.1	0.2	19.5	19.6	50.3	53.2	7.5	2.8	2.3	2.4	2.4	2.5	2.6	2.6
Net Income	**3.3**	**3.9**	**1.2**	**3.3**	**305.3**	**307.8**	**788.8**	**832.8**	**118.1**	**43.8**	**36.8**	**37.5**	**38.3**	**39.0**	**39.8**	**40.5**
EPS	1.86	1.94	0.58	1.65	152.64	153.90	394.40	416.42	59.04	21.92	18.40	18.76	19.13	19.50	19.88	20.27
S/O	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Cash Balance				-30	276	276	1,064	1,897	2,015	2,059	2,096	2,134	2,172	2,211	2,251	2,291
Debt				0	0	0	0	0	0	0	0	0	0	0	0	0
Net Cash	0	0	0	-30	276	276	1,064	1,897	2,015	2,059	2,096	2,134	2,172	2,211	2,251	2,291
Gross Margin				91%	99%	99%	100%	100%	97%	68%	-212%	-203%	-194%	-185%	-177%	-169%
OPEX				20%	3%	3%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
R&D				0%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
S&M				0%	1%	1%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
G&A				20%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Operating Income				71%	97%	97%	98%	98%	97%	68%	-212%	-203%	-194%	-185%	-177%	-169%
Net Income				67%	91%	91%	92%	95%	130%	469%	3825%	3786%	3748%	3710%	3672%	3635%

Debt
Coupon

Equity
Share Px
0.0 New Shares
2.0 S/O

0 Total Raise
30 Purchase Px
Multiple

Discount
2,028 NPV

TURING
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Project Dart

June 2015

TURING
PHARMACEUTICALS

Project Dart

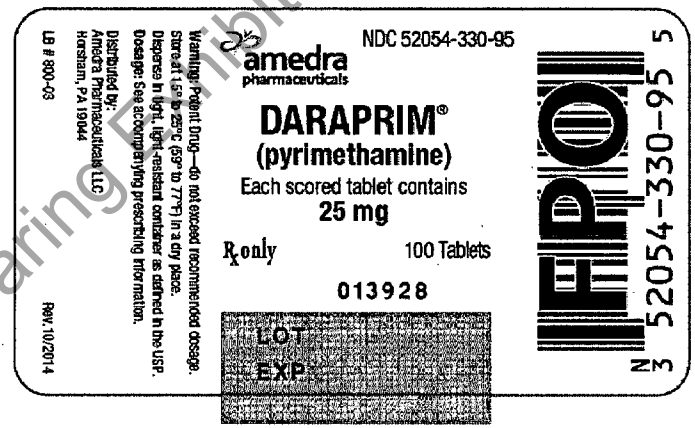
June 2015

Executive Summary

- **Turing is in discussions to acquire Daraprim® (pyrimethamine) from Impax Labs (IPXL)**
  - 2014 US net revenue of $4.9mm
  - Initial offer of 6x 2014 US net sales ($29.5mm)
- **Daraprim® is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide, since synergism exists with this combination**
  - FDA approved in January 1953 (NDA #008578)
  - Gold standard of care for toxoplasmosis
- **Turing is looking to borrow $5mm – $15mm in senior secured debt**
  - The transaction will be financed with a combination of debt and equity
- **We believe there are several potential strategies to grow revenue**
  - Current pricing lower than other adjunctive therapies
  - Daraprim® fits the specialty distribution business model

Daraprim Prescribing Information and Pricing

- **Daraprim® is indicated for the treatment of toxoplasmosis encephalitis**
  - Approved January 23, 1953
  - No approved generics or recent DMFs
- **Current gold standard for Toxoplasmosis**
  - Co-administered with sulfadiazine
  - Inhibits DHFR, disrupting folate synthesis
- **Dose: 50 – 75mg/day**
  - 25mg, 100 count bottle
  - ~$3,000 PPPY
- **Payor Mix**
  - 45% Commercial
  - 25% Medicaid
  - 25% Medicare Part D
  - 5% Cash



Actual	2011	2012	2013	2014	Q1:2015
Units (bottles)	12,600	11,004	10,260	9,708	1,836
Net Sales (mm)	$5.114	$5.620	$5.829	$4.932	$1.226

Gross-to-Net Calculation

- **Chargebacks are specific to Impax's current contracts with group purchasing organizations (GPOs) and managed care**
  - Current pyrimethamine chargeback terms likely a result of negotiated terms for a larger Impax portfolio

	2011	2012	2013	2014	Q1:15
Gross Revenue	9,138,946	10,650,678	12,067,428	13,146,270	2,488,661
Cash Discount	182,779	213,014	241,348	256,317	51,003
Medicaid	1,104,817	1,812,187	2,878,267	3,348,557	699,472
Returns	673,025	532,534	241,176	1,061,405	(72,997)
Rebates	612,949	746,747	683,141	864,634	183,242
Discount Rebate	-	-	10,056	9,765	2,290
Chargebacks	1,450,864	1,725,553	2,183,854	2,673,073	398,986
Net Revenue	**5,114,512**	**5,620,644**	**5,829,586**	**4,932,521**	**1,226,665**
Units	12,576	11,004	10,260	9,708	1,836
Px/unit	727	968	1,176	1,354	1,355
Realized Px/unit	407	511	568	508	668
Cash Disc	2.0%	2.0%	2.0%	1.9%	2.0%
Medicaid	12.1%	17.0%	23.9%	25.5%	28.1%
Returns	7.4%	5.0%	2.0%	8.1%	-2.9%
Rebates	6.7%	7.0%	5.7%	6.6%	7.4%
Dis Rebate	0.0%	0.0%	0.1%	0.1%	0.1%
Chargebacks	15.9%	16.2%	18.1%	20.3%	16.0%
Net Revenue	56.0%	52.8%	48.3%	37.5%	49.3%

Toxoplasmosis Overview

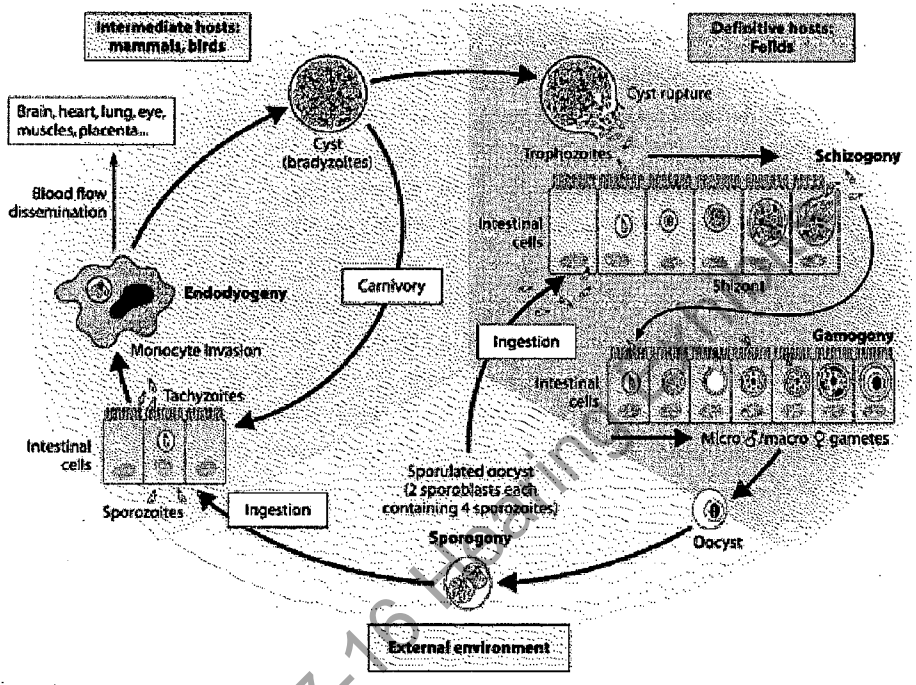


FIG 2 Life cycle of *Toxoplasma gondii*. Shown are the biology, infection, and replication of the three infective stages of the parasites in their respective hosts.

- Approximately 15% of US population is seropositive for toxoplasmosis (30% worldwide, >50% in Brazil)
- Patients become infected by ingesting cysts in undercooked pork or oocysts in contaminated water
- Toxoplasmosis can cause severe neurological, ocular, and systemic diseases in neonates and individuals with weakened immune systems
- Symptoms self-resolve in immunocompetent hosts, though cysts containing dormant bradyzoites will remain throughout life, predominantly in the brain, CNS and musculature

<u>Toxoplasmosis is always life threatening for neonates and the immunocompromised</u>

Toxoplasmosis Clinical Presentation

Immunocompromised Patients

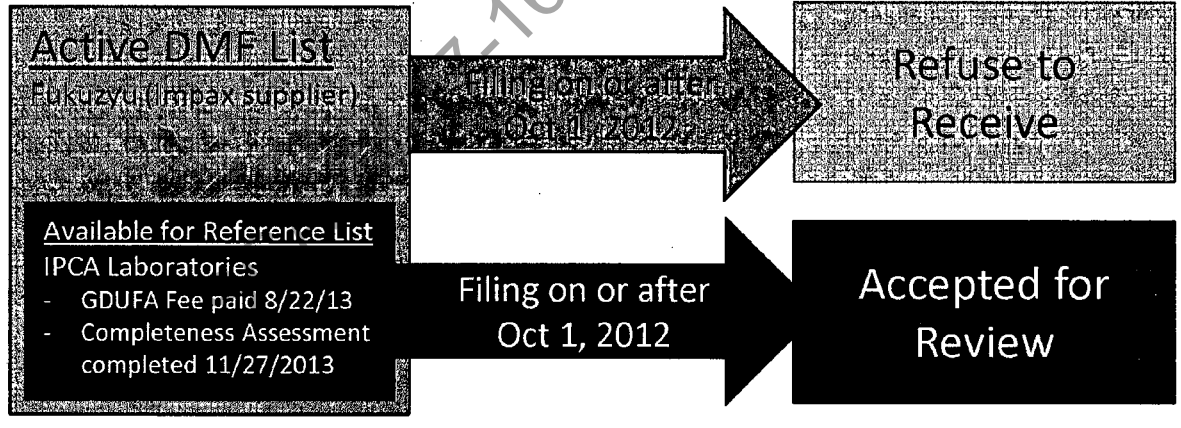
- Majority of patients are HIV positive with CD4+ counts < 100
  - Occasional incidence in immunosuppressed transplant patients
- Initially presents with non-specific symptoms such as headache, lethargy, and fever
- Disease is usually identified when patients present with difficulty walking, weakness on one side of the body (hemiparesis), seizure, speech abnormalities and loss of memory
- If untreated, further cerebral necrosis leads to dementia, status epilepticus, coma and death
- Primary lesions of cerebral necrosis, but retinal lesions are common if the infection disseminates to the eye, which can lead to blindness

Congenital Toxoplasmosis

- Estimated incidence of 1:10,000 births
- Risk of infection increases with each trimester, but infections in the first trimester lead to the most severe disease
- Congenital infection can lead to a wide variety of manifestations including spontaneous abortion, hydrocephalus or microcephalus, CNS calcification, retinochorioditis, and failure to thrive
- Symptoms that present later in infancy and childhood include learning disabilities, growth retardation, mental retardation, convulsions, palsies, blindness and deafness

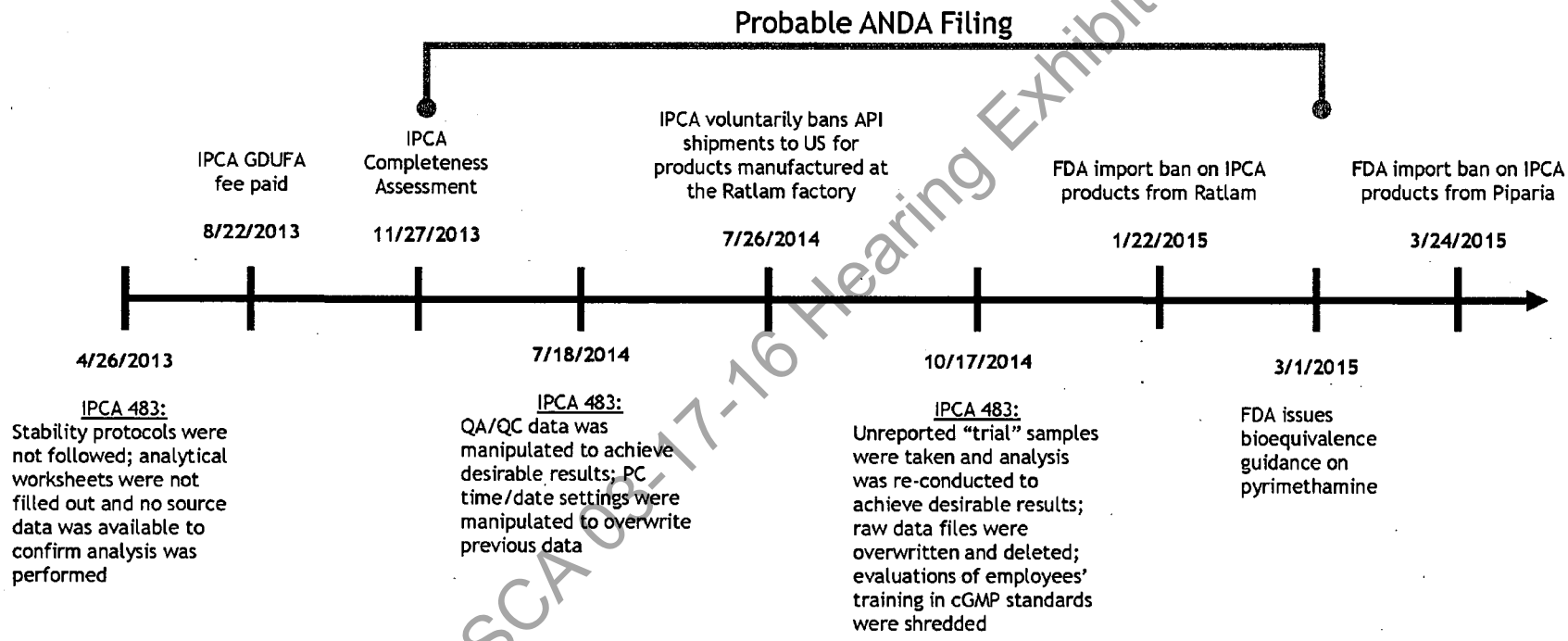
New Entrant Feasibility

- Under GDUFA, ANDAs filed on or after October 1, 2012 referencing Type II DMFs must use a DMF listed on the "Available for Reference" list to avoid receiving a "Refuse to Receive" response from FDA
- Turing believes an ANDA was likely filed in 2014 using IPCA's API
  - FDA released bioequivalence guidance for pyrimethamine in March 2015, likely in response to an earlier filing
  - Fukuzyu currently in an exclusive supply agreement with Impax and not listed as "Available for Reference"



New Entrant Feasibility

- IPCA's <u>data integrity issues</u> are likely to cause significant disruption to any filing



New Entrant Feasibility

- **Data Integrity is a very important issue for FDA**
  - IPCA will have to conduct very rigorous review of data reporting standards
  - Any ANDAs currently on file will likely be put on hold
- **Potential filer may stay with IPCA**
  - IPCA has confirmed that they will be unable to supply pyrimethamine for at least 12 months
    - Independent consultants believe this timeline is "very aggressive"
  - Citizens petition could further delay any ANDAs filed with IPCA supply
  - There is no protocol for lifting import bans, which may delay process further
- **Potential filer may have moved to a new vendor**
  - Appearance in the "Available for Reference" list will signal the refiling/amendment
  - Filer will need to requalify any API and re-validate processes and methods
  - Additional 6 months minimum for long term and accelerated stability
  - Major amendment to ANDA will further delay review date
  - FDA may allow filing without additional bioequivalence
- **Turing believes Daraprim will remain sole source until at least mid 2016**
- **If no developments have occurred by 2016, Turing believes Daraprim could remain a single source product much longer**

Lifecycle Management

- **Line extensions**
  - Once-a-day pill
  - Combination with sulfadiazine
- **Next generation analogues**
  - No new medicines have been approved in more than 40 years
  - Improved potency, avoid teratogenicity
  - Target T. gondii DHFR
    - Pyrimethamine more active against human DHFR
- **Toxoplasmosis Vaccine**
  - Academics have made progress in several vaccines targeting various surface antigens
    - SAG1

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Experienced and Fast-Growing Commercial Team

Executive	Experience
Nancy Retzlaff *Chief Commercial Officer*	• More than 20 years of biopharmaceutical commercial leadership experience including sales, marketing, commercial development & business leadership roles at Bayer, Schering-Plough, Pfizer & Mesoblast
Richard DeYoung *Head of Sales & National Accounts*	• More than 15 years of biopharmaceutical experience leading sales, key accounts and managed markets teams at Takeda and Astra Zeneca
Tina Ghorban *Senior Director, Business Analytics & Customer Insights*	• 15 years of biopharmaceutical experience in market analytics, global commercial development, new product marketing and US marketing at Pfizer, Shionogi and Mesoblast
Scott Emmens *Sales Director*	• 15 year biopharmaceutical sales leadership experience including sales operations and sales training at Astra Zeneca, Takeda and Shire

Relevant Experience and Skill Sets:

- Therapeutic areas of expertise include orphan & rare diseases and broader disease areas (HIV, pain, IBD, anemia, diabetes, cardiovascular, respiratory, endocrinology, CNS)
- Experience across broad range of product lifecycles, including global and US launches, mature brands, peri-LOE and branded generics
- Creation of complete commercial organization and infrastructure, as well as leading organizations through dynamic change and growth
- Alignment of marketing & sales around a specialty distribution strategy and patient services platform
- Creation of strategic brand platform, market development plan, and communication platforms. Tactical execution of all planned activities.
- Strategic planning and execution with all key customers, including KOLs, physicians, payers, patients and patient advocacy

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Financial Projections

- **Toxoplasmosis is a rare disease and should be priced appropriately**
  - Current Hepatitis C cost for cure > $100,000
  - Net present value of HIV treatment > $250,000
  - Both significantly more prevalent and have multiple treatment options
- **Turing management has experience with similar revenue growth strategies while at Retrophin**
  - Specialty sales force
  - High-touch closed distribution system
  - Improved patient advocacy and support
- **Potential revenues of over $500mm with greater than 80% EBITDA margins**
- **Turing plans to finance the transaction with a combination of debt and equity**

Financial Model

- **Illustrative Model**
  - Assumes $200,000 per unit

	2011	2012	2013	2014	Partial 2015	Full 2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Net Revenue (mm)	**5.1**	**5.6**	**5.8**	**4.9**	**336.5**	**339.2**	**854.7**	**880.4**	**90.7**	**9.3**	**1.0**	**1.0**	**1.0**	**1.1**	**1.1**	**1.1**
Total COGS	0.6	0.5	3.6	0.4	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Gross Profit	4.5	5.1	2.2	4.5	333.5	336.2	851.7	877.4	87.7	6.3	-2.0	-2.0	-2.0	-1.9	-1.9	-1.9
R&D	0.0	0.0	0.0	0.0	4.0	4.0	4.0	4.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sales Force	0	0	0	0	30	30	30	30	0	0	0	0	0	0	0	0
FTE Salary	0.0	0.0	0.0	0.0	0.250	0.250	0.253	0.255	0.258	0.260	0.263	0.265	0.268	0.271	0.273	0.276
Sales & Marketing	0.0	0.0	0.0	0.0	3.8	3.8	7.6	7.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
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OPEX	1.0	1.0	1.0	1.0	8.8	8.8	12.6	12.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
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Debt				0	0	0	0	0	0	0	0	0	0	0	0	0
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R&D				0%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
S&M				0%	1%	1%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
G&A				20%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
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Net Income				67%	91%	91%	92%	95%	130%	469%	3825%	3786%	3748%	3710%	3672%	3635%

0 Debt
0% Coupon

0 Equity
0 Share Px
0.0 New Shares
2.0 S/O

0 Total Raise
30 Purchase Px
5.0X Multiple

15% Discount
2,028 NPV

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June 2015

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Assessing The Market Potential For Sulfadiazine And Pyrimethamine

June 10, 2015

Table of Contents

Objectives and Methodology

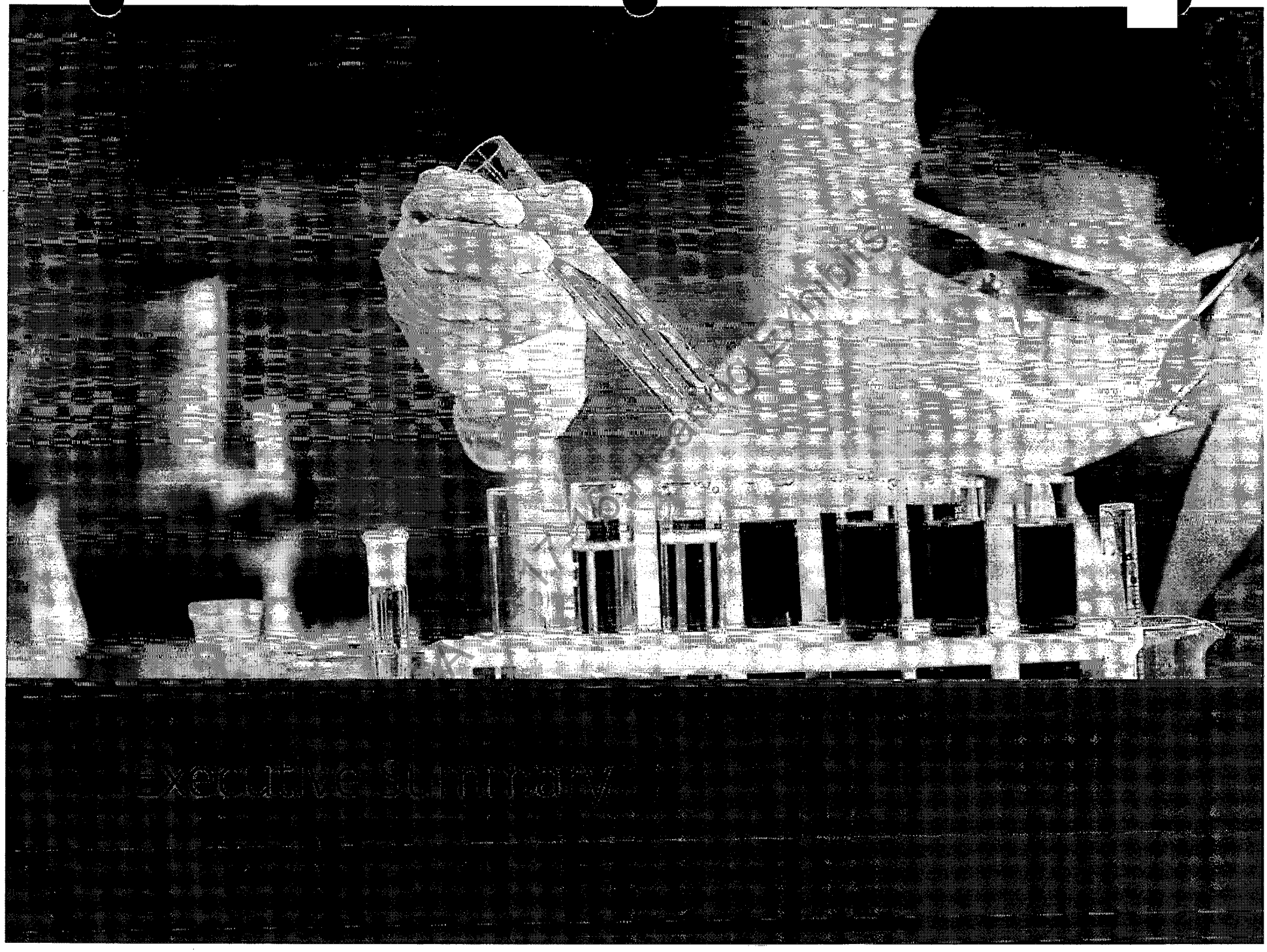
Business Objective:

- Evaluate the potential to preserve the value of sulfadiazine and/or pyrimethamine for the treatment of toxoplasmosis in the event of an increase in the cost of these agents.

Research Objectives:

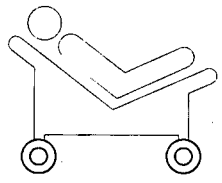
- Clarify the toxoplasmosis treatment algorithm and considerations in selecting therapies
- Identify differences in approach for specific patient sub-populations
- Determine the impact of cost on treatment decisions by sub-population
- Explore opportunities to enhance the value of sulfadiazine and/or pyrimethamine in the treatment of toxoplasmosis, *e.g.* lifecycle strategies and partnerships

Physician Telephone Depth Interviews - May 20, 21, 22, 2015					
Infectious Disease	Pediatric Infectious Disease	PCP's	Internal Medicine	OB/GYN	TOTAL
7	1	2	5	2	17



executive summary

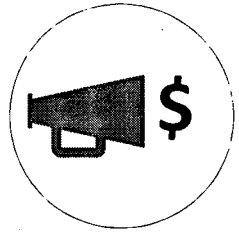
Toxoplasmosis Treatment Context



Mostly seen in HIV patients who are often non-compliant; may wait until treatment is critical

Typically present to hospital ER and are admitted

All patients referred to Infectious Disease (ID) specialist



IDs will advocate for the standard of care, even if it's costly

compliance

is the largest barrier to treatment

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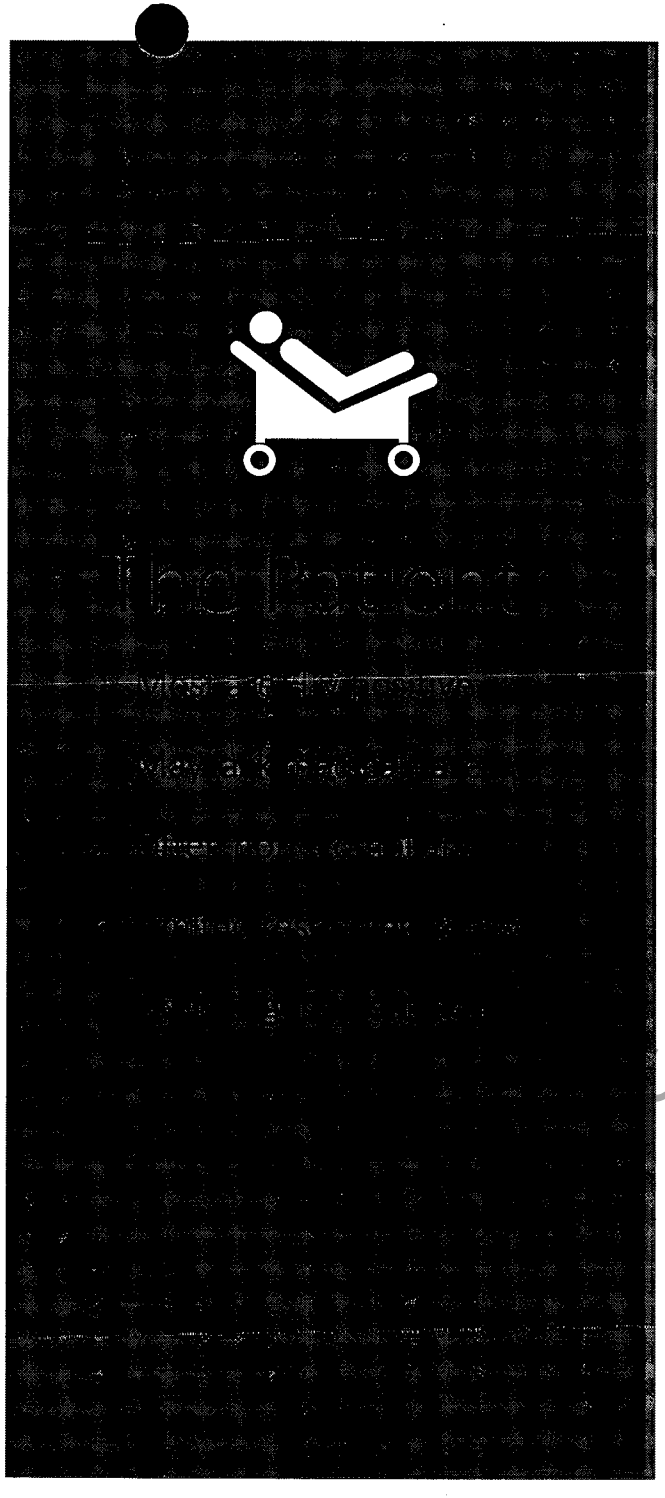
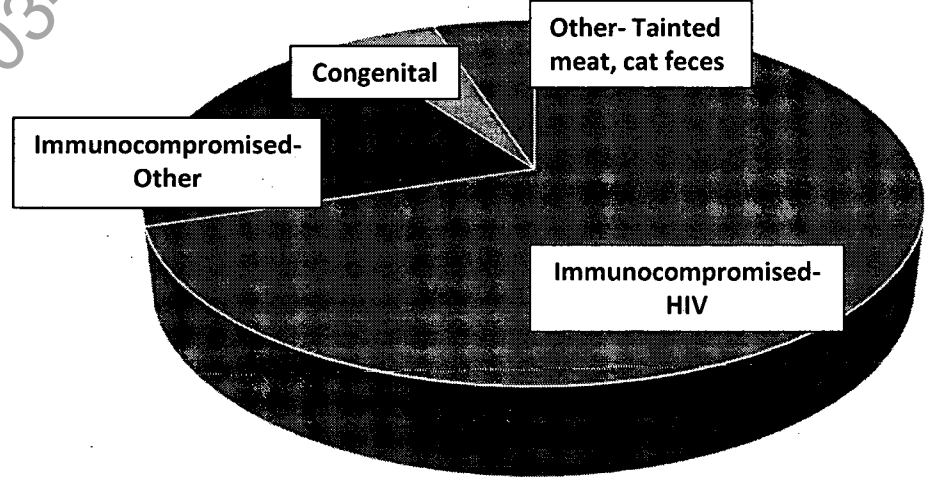
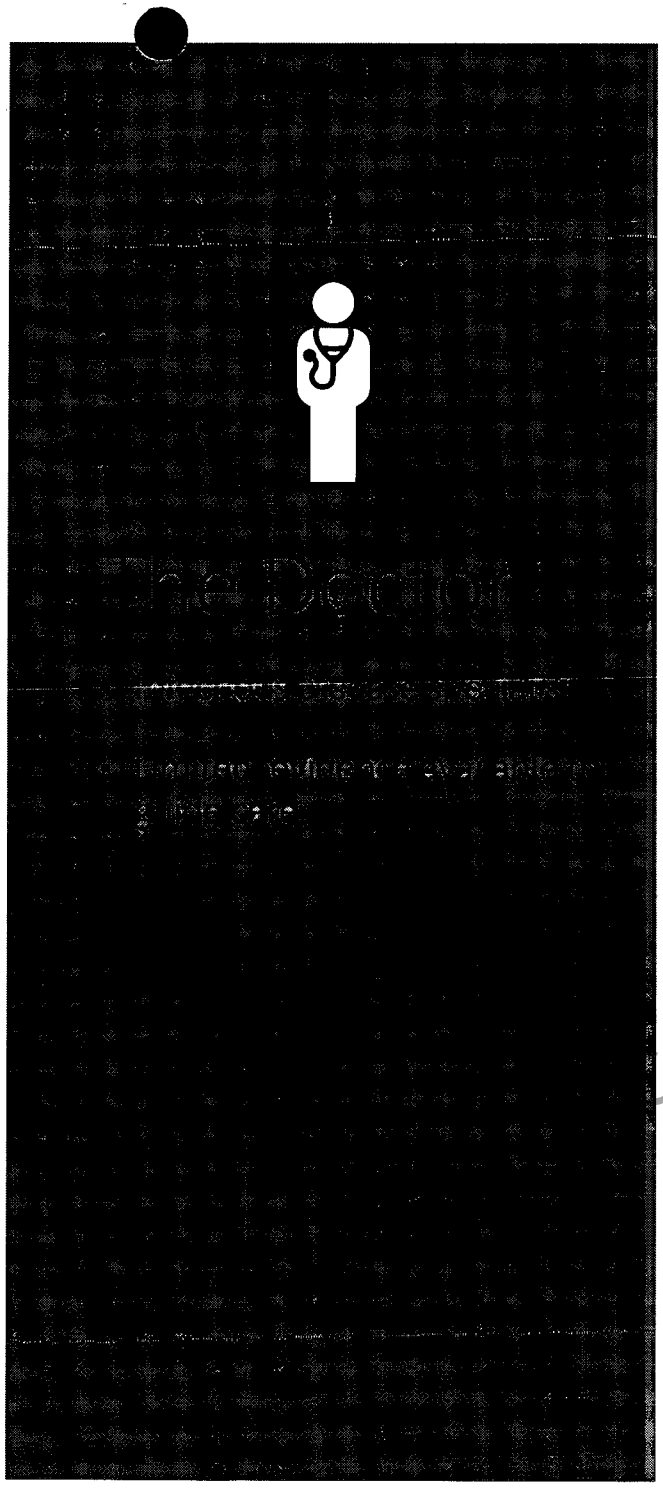
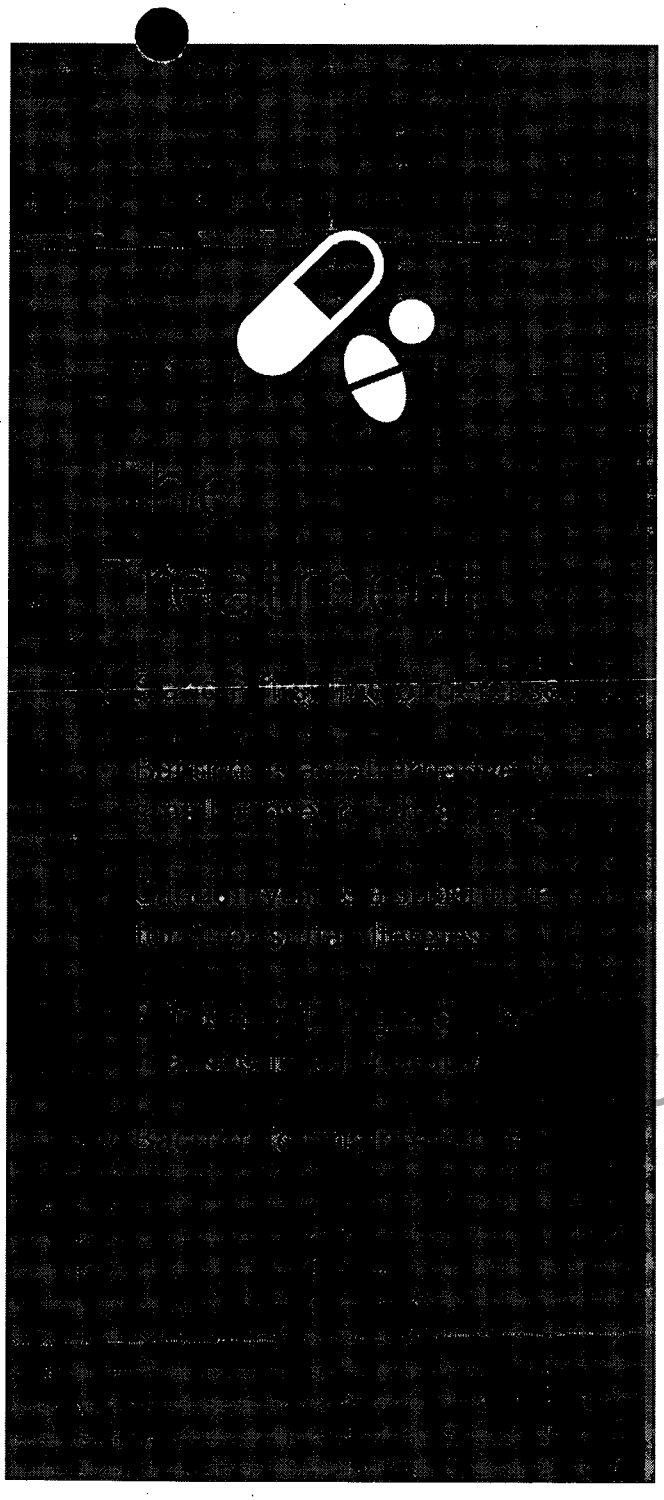


- The majority of toxoplasmosis (toxo) cases are seen in HIV-infected patients. In many cases, these are patients who:
  - Have not sought regular medical care with the result that diagnosis and treatment of HIV and opportunistic infections may have been delayed
  - Struggle to comply with long-term and/or complex preventive medication regimens
  - Have limited ability to pay for treatment
- Incidence is perceived to be decreasing as improved HIV treatments have resulted in relatively stable immunity today
- The need to treat is considered urgent in all types of cases with the goal of stabilizing disease, not eradicating it, and treatment is often initiated in-hospital



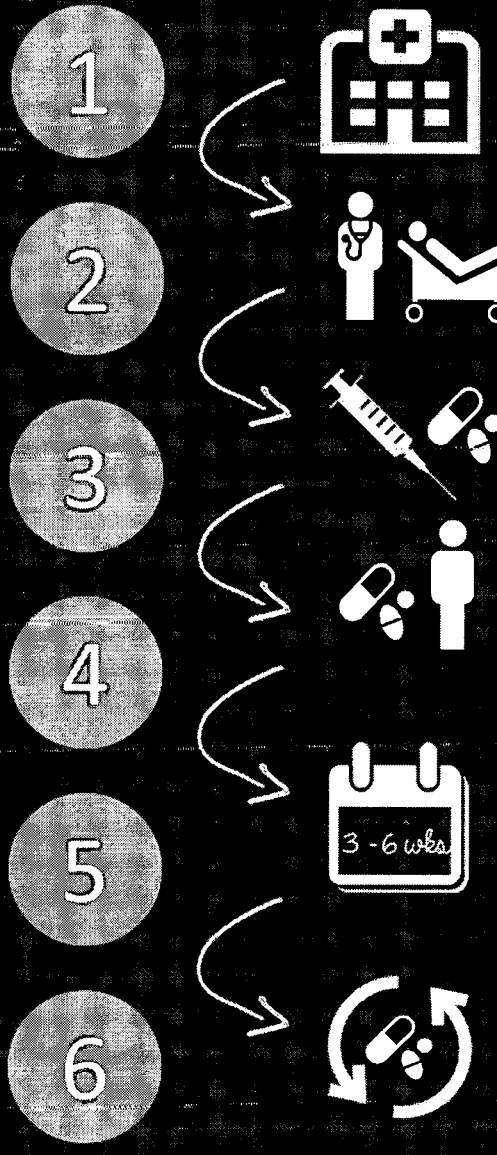


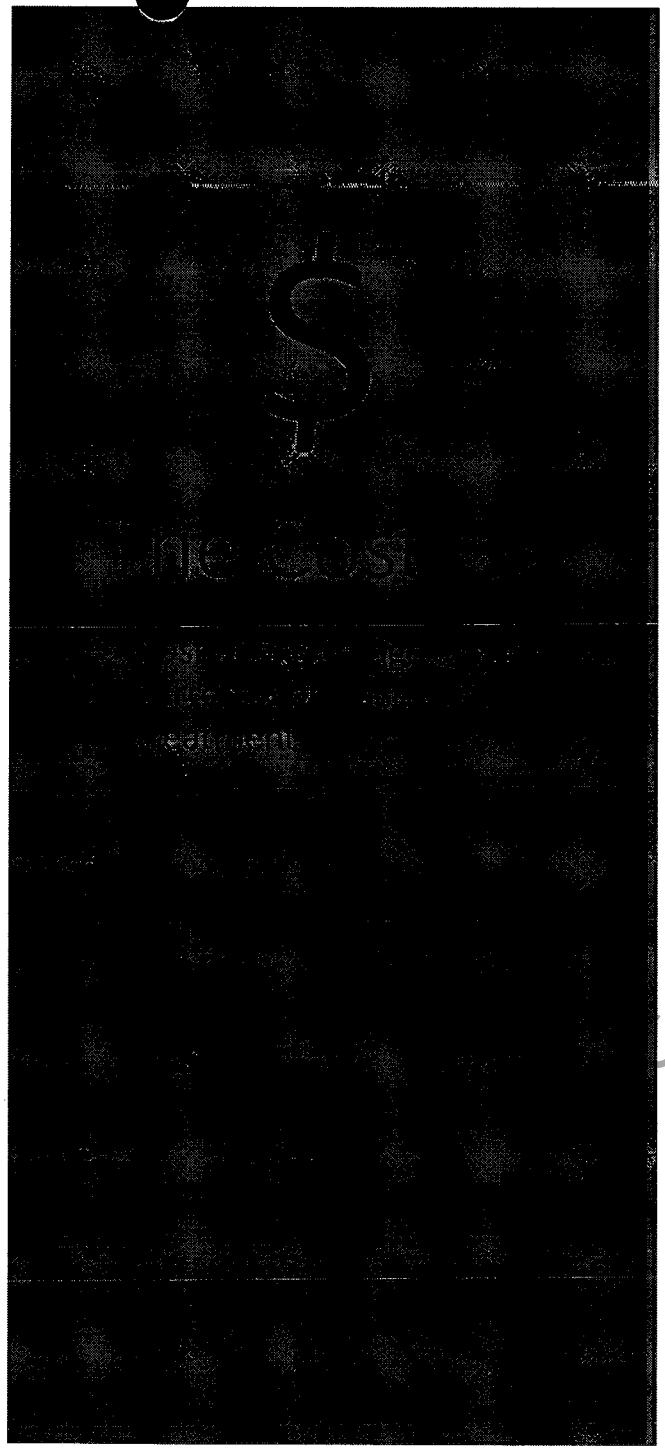
- Treatment is commonly initiated by infectious disease specialists (IDs)
- Poor clinical evidence is available to guide treatment of toxo; most physicians reference CDC, NIH and IDSA guidelines for managing toxo in HIV patients, expert opinion, and personal experience
  - With fewer opportunistic infections in the population, newer treatments are not being developed, and guidelines have not been updated or amended to address non-HIV populations



- Regardless of the treatment setting, nearly all physicians prescribe sulfadiazine (S) and pyrimethamine (P) first line for all types of toxo cases
  - Response is often seen in 2-3 weeks
  - For HIV patients, acute treatment usually lasts 3-6 weeks
  - Bactrim is an alternative first line treatment for a very small subset of physicians who may tend to be younger and prefer the simplicity and cost advantages of a combination pill
- Clindamycin is the primary substitute for S in patients exhibiting a sulfa allergy
- P tolerability is good, and side effects are rarely observed; thus it is a "backbone" of therapy and not often substituted
- Bactrim is preferred for prophylaxis in HIV patients and as maintenance therapy in all patients who require it
  - Fixed dose combination supports compliance and is relatively inexpensive – both important for long-term use

Typical Toxoplasmosis Treatment Flow



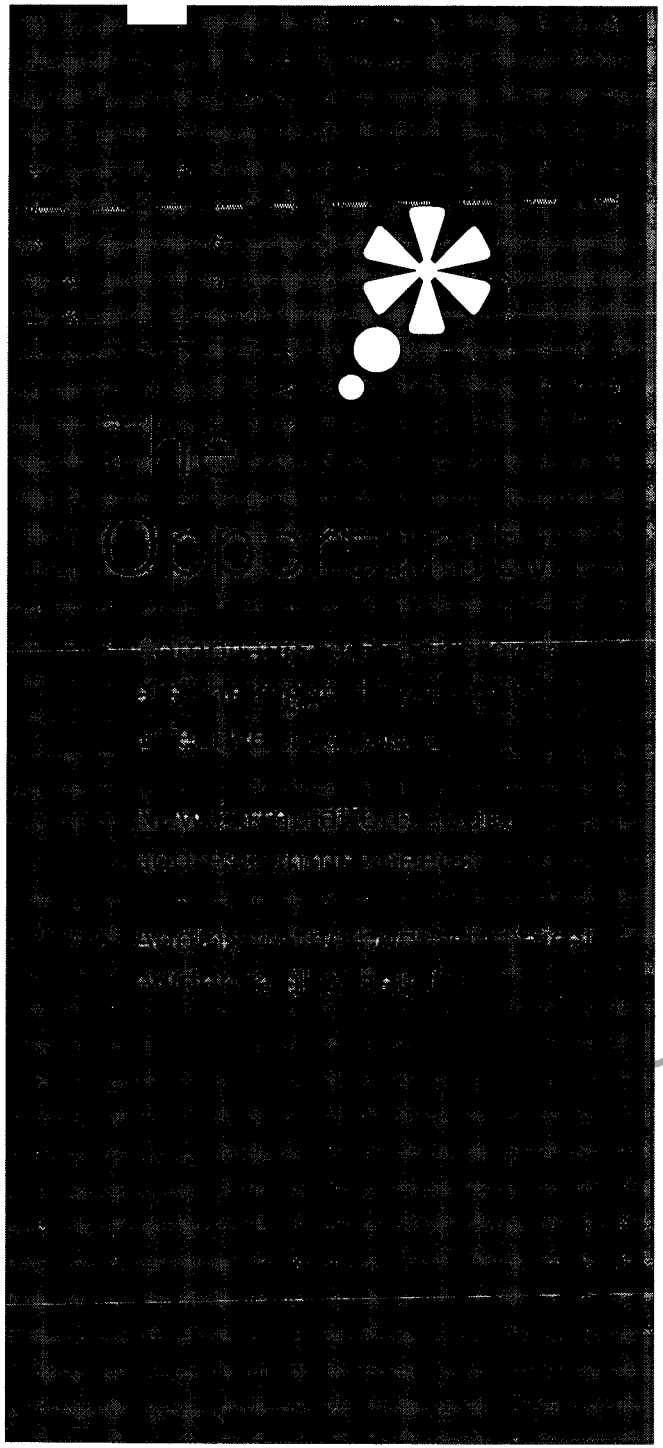


COST CHALLENGES

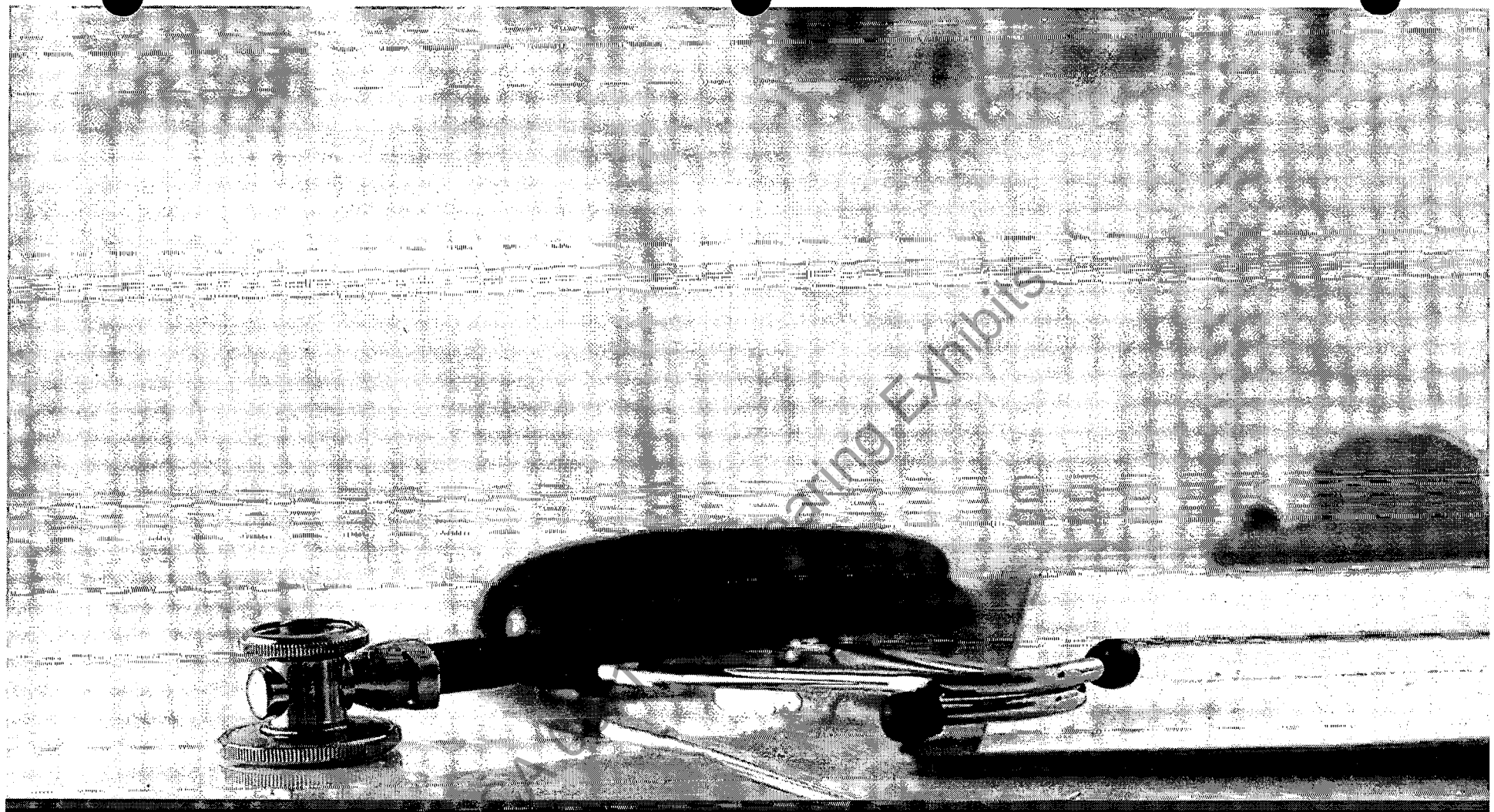
- Physicians would prefer not to have to substitute another drug for S or P due to cost
- Most physicians would complete prior authorizations or pursue financial support in the interest of securing "gold standard" treatment for patients

TRADE-OFFS

- If patients were to decline the "best" therapy due to cost, physicians would reluctantly prescribe their 2L alternative to S
  - Would expect and be resigned to decreased efficacy
  - Sub-optimal therapy would be considered better than no therapy
- Physicians are at a loss to think of an appropriate alternative to P



- Fixed dose combinations of S and P are a "*no brainer*" to help improve compliance
  - Multiple combinations would be required for acute versus maintenance dosages and to accommodate differences in the recommended dosing frequency of each
  - Pill size may be an issue
  - Extended release formulations (*e.g.*, one injection per month) would also address compliance issues
- S and P in an IV formulation could be useful for NPO patients in-hospital
- Resources/services to support medication adherence could be useful, especially those that utilize technology, *e.g.* a digital monitoring device on pill bottle cap
- New Level I evidence about optimal treatment of toxo is needed, especially head-to-head studies, but it may be extremely difficult to enroll appropriate populations in numbers sufficient for randomized control trials



Comments on Hearing Exhibits

Cost Perception

Conclusion

As the clinicians primarily responsible for toxo treatment, IDs are not cost- or price-sensitive

- Highly focused on therapeutic benefit
- Think current cost of pyrimethamine + sulfadiazine is more expensive than other 2L therapies already but consider it the gold standard nonetheless
- Will take action to secure "best" treatment for patients

Recommendation

Enhance the S+P value proposition and offset perceptions of high cost

- Make the regimen affordable with a Patient Assistance Program for patients unable to pay

Patient Needs

Conclusion

Patient compliance is the biggest obstacle to effective treatment

- Compliance with a complicated regimen
- Adherence over a long period, possibly a lifetime
- Long-term out-of-pocket expense

Recommendation

Make the regimen easier for compliance

- Medication reminder platform
- New formulations and packaging, *e.g.* combination pills, extended release formulations, combination blister packs, IV formulations, etc.

Support for the Standard of Care

Conclusion

Although current guidelines are clear, evidence supporting S+P is limited

- Currently limited to HIV primarily
- All physicians, and IDs in particular, value clinical data and would be receptive to new information

Recommendation

Deepen ID commitment to the <u>standard of care</u>

- Invest in a retrospective analysis of cases or an expert panel review regarding toxo treatment and outcomes in HIV and other affected populations

Payer Strategy

Conclusion

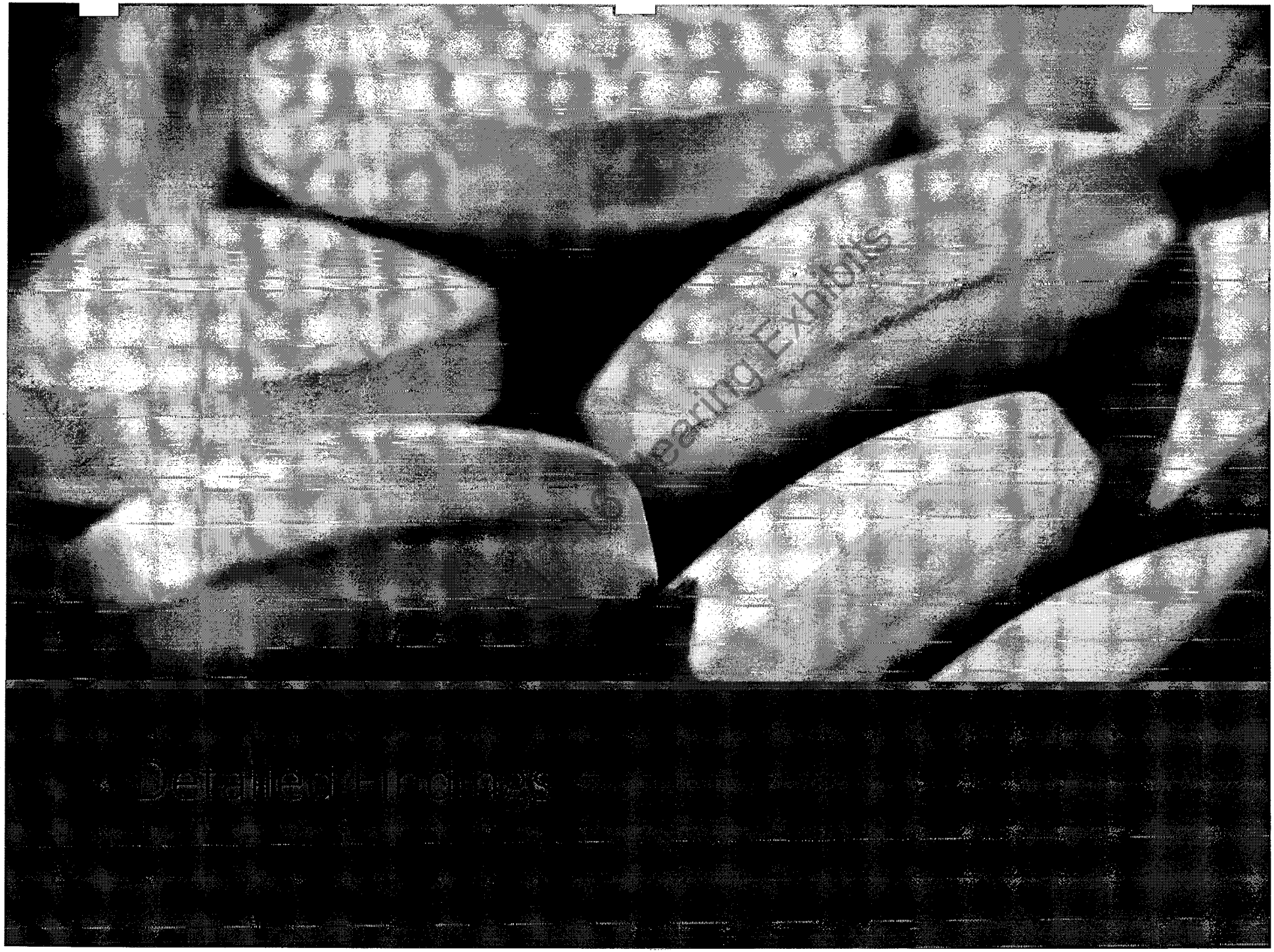
Commercial and public payers do not appear to scrutinize pricing of toxo drugs today

- Low incidence disease
- Out-of-pocket burden is not an obstacle for most patients, despite payer ability to cost shift or eliminate access altogether

Recommendation

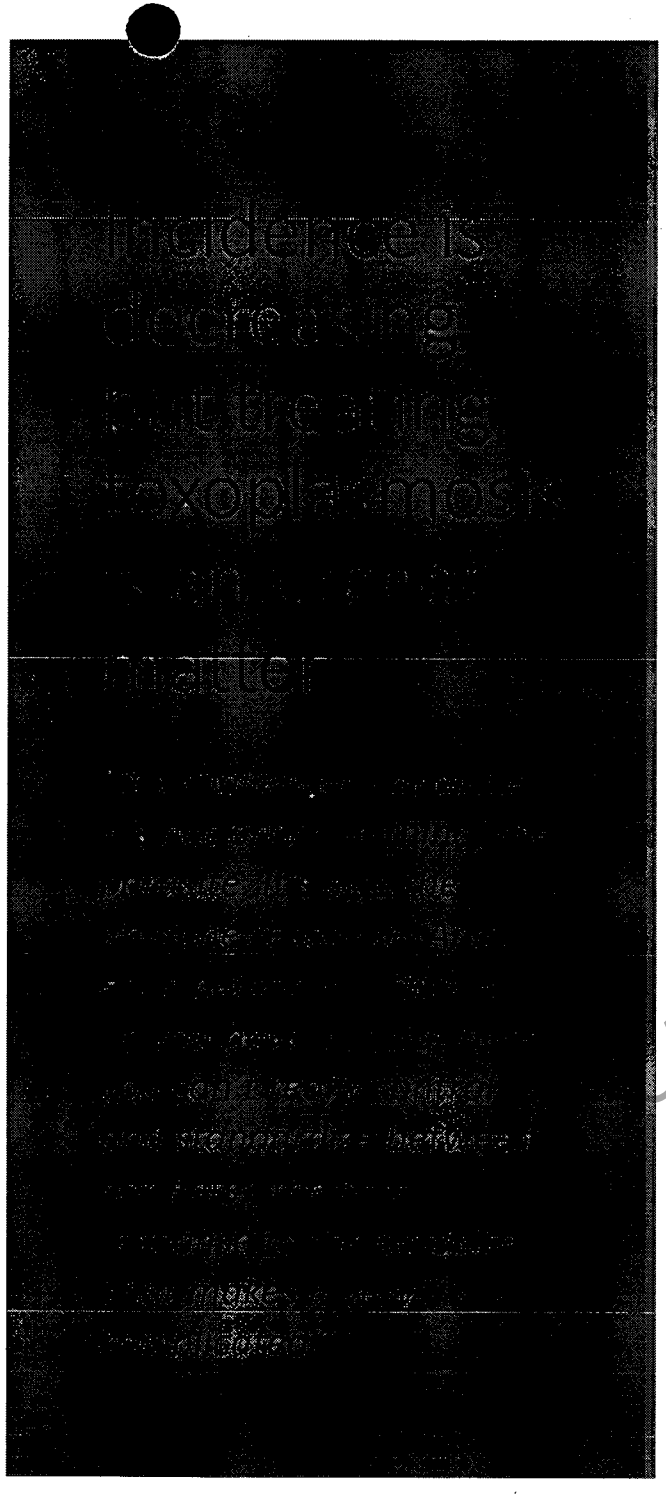
Formulate and implement a <u>payer strategy</u>

- Conduct market research among commercial payers to assess the potential impact of various pricing scenarios
- Consult experts to understand Medicaid pricing and the impact of price increases

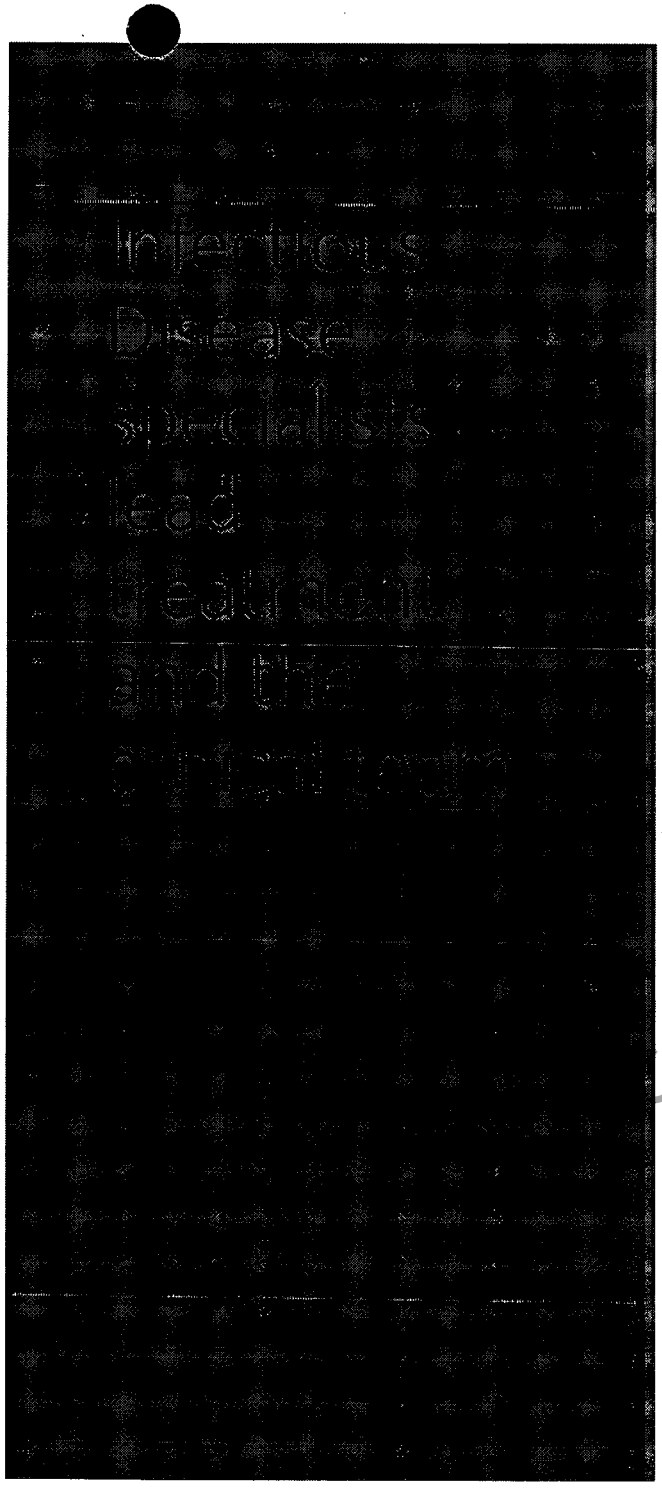

Detailed Images

TREATMENT ENVIRONMENT

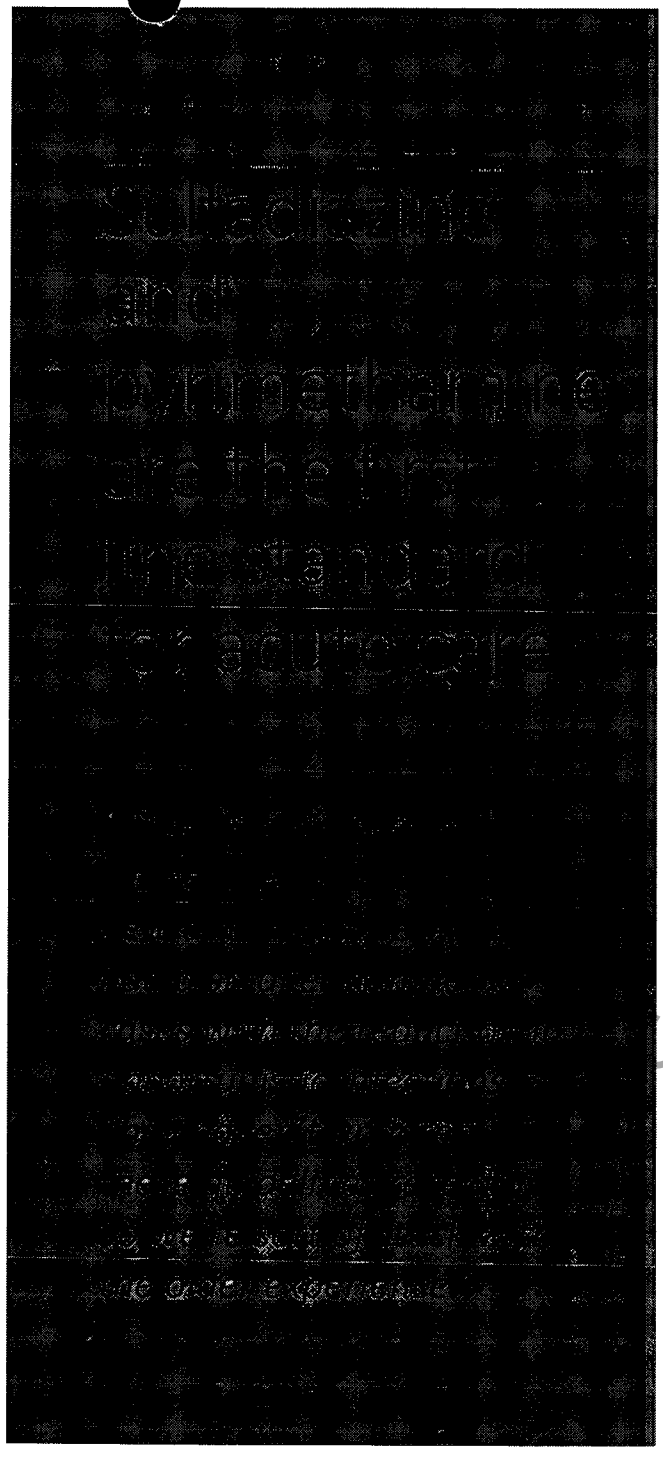
TURING
PHARMACEUTICALS



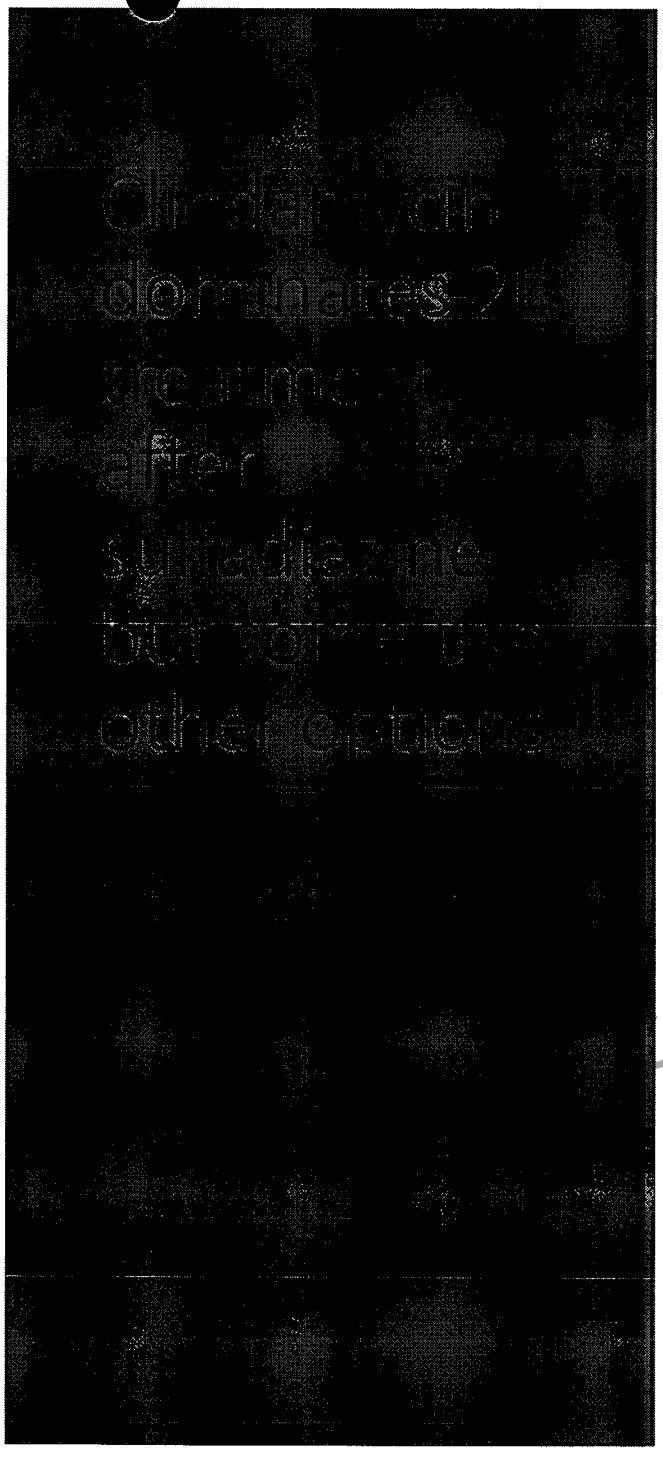
- The vast majority of toxoplasmosis cases are seen in HIV-infected patients, followed by (in order of frequency of mentions):
  - Other immunocompromised patients such as transplant patients and patients on chemotherapy
  - Retinitis
  - Immunocompetent patients
  - Congenital
  - Pregnancy
- Incidence is perceived to be decreasing as improved antiretroviral therapy and widespread use of Bactrim as prophylaxis (in HIV patients with CD4 counts <200) result in relatively stable immunity today
- The need to treat is considered urgent in all types of cases, and treatment is often initiated in-hospital
- Goals of treatment are stability and control, not eradication, as disease often recurs



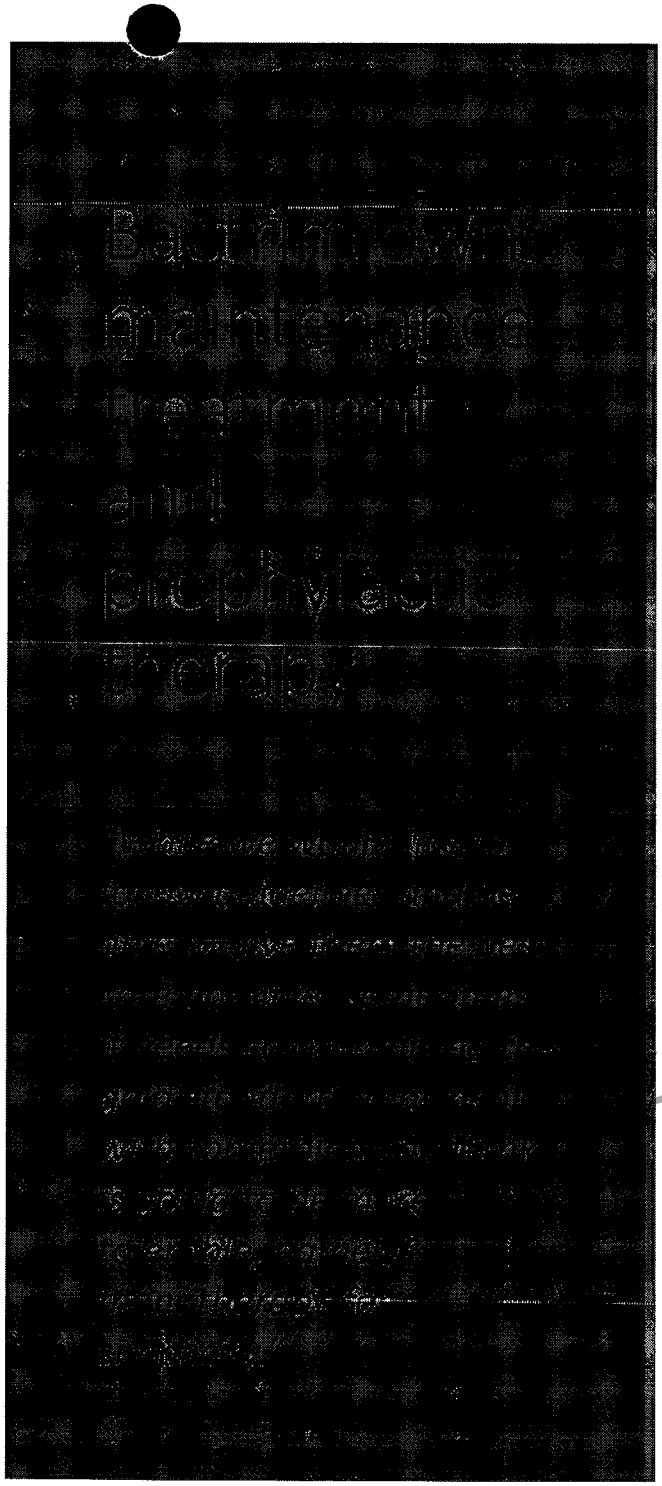
- Patients experiencing serious symptoms may present in the ER or be immediately recommended for admission by their outpatient physician
- PCPs, IMs, and ob/gyns typically refer to an infectious disease specialist (ID) when a diagnosis is suspected or confirmed via imaging studies, PCR testing, or IgG and IgM testing
- Treatment is most commonly initiated by infectious disease specialists (IDs) in both the inpatient and outpatient settings
  - Other physicians may be involved in co-management and monitoring, especially during the maintenance phase of therapy



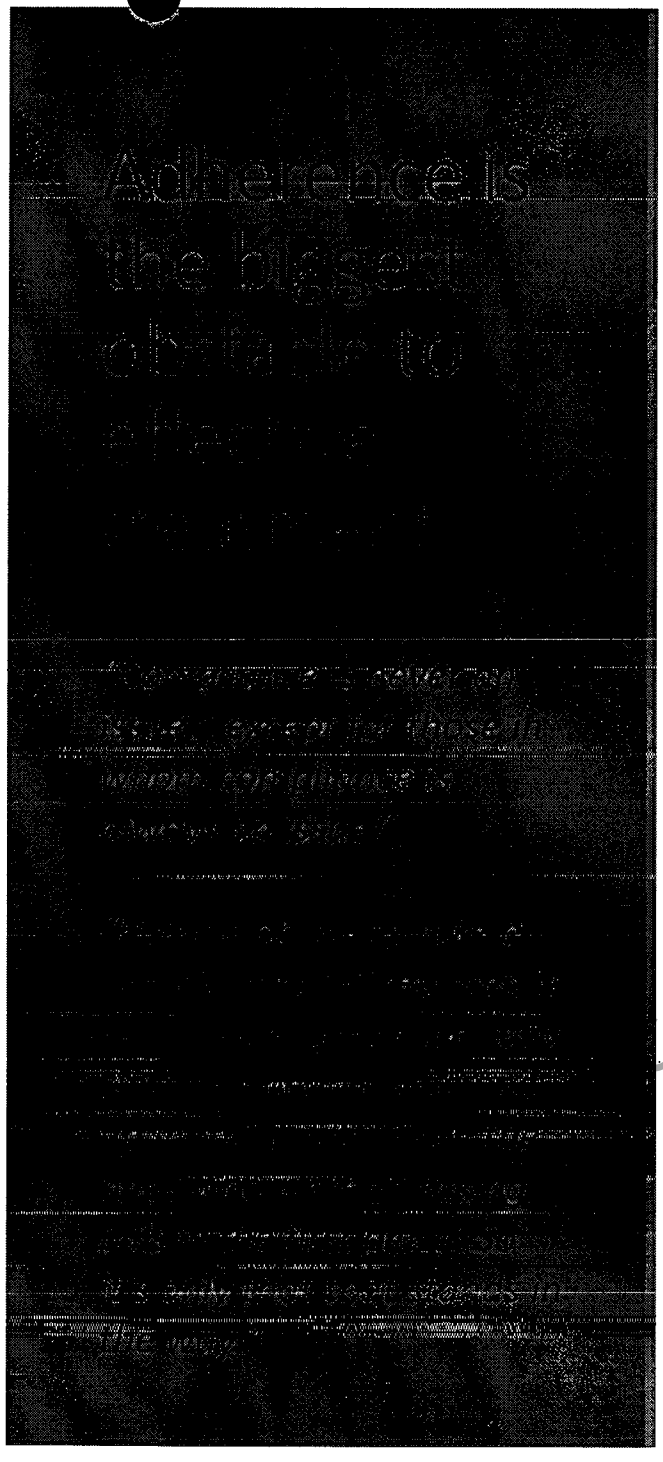
- Regardless of the treatment setting, nearly all physicians prescribe sulfadiazine and pyrimethamine for all acute patients
  - Consistent with CDC and NIH guidelines for managing toxo in HIV patients which are generalized to other populations
  - Bactrim is an alternative first line treatment for a very small subset of physicians who may tend to be younger and prefer the simplicity and cost advantages of a combination pill
  - Leucovorin is used concomitantly in HIV patients
  - Although not commercially available in the U.S., spiramycin is recommended for infected women <18 weeks into their pregnancy, and S+P is recommended for infected women >18 weeks into their pregnancy
  - For congenital cases, S+P or Bactrim may be used
- Many perceive S+P to offer efficacy superior to other options but physicians acknowledge limited Level I evidence is available
- Perception is that sulfadiazine may be delivered intravenously to inpatients (although an IV formulation is not commercially available); patients are discharged with prescriptions for oral S+P
- Patients are typically treated with S+P for 3-6 weeks, when symptoms may be lessened or resolved and/or imaging reveals brain and/or eye lesions have shrunk in size



- For patients exhibiting a sulfa allergy or side effects, clindamycin is the primary second line treatment substituted for sulfadiazine
  - Although clinical evidence is poor, clinda thought to offer efficacy inferior to sulfadiazine despite patients progressing well on it
- Pyrimethamine is generally well-tolerated, and substitutions do not appear to be necessary
- Second or third line alternatives to S, especially in those who don't tolerate clinda or do not respond to treatment, include:
  - Atoquavone
  - Dapsone
  - Zithromax
  - Possibly high dose Bactrim



- After the acute phase of toxo treatment, HIV patients are routinely transitioned to Bactrim for maintenance, sometimes even before full treatment regimen of S+P is complete
  - Convenient combination regimen is inexpensive and straightforward relative to S+P
  - Broad spectrum antibiotic protects against other opportunistic infections
  - HIV patients will continue until CD4 counts are >200 for at least six months and possibly for a lifetime
- Post-acute therapy for non-HIV patients is lower doses of S+P or therapy may be discontinued depending on clinical and radiologic evidence of remission/ongoing disease
- Bactrim is commonly used as prophylactic therapy to prevent pneumocystis pneumonia in HIV patients with CD4 counts < 200
  - Prevention of toxo is a side benefit; "*two birds with one stone*"



- S+P comprises a difficult regimen, especially for HIV patients taking multiple medications.
- "Medication exhaustion" stems from:
  - A frequent and complicated dosing regimen
    - S is QID, P is TID
  - Difficulty swallowing multiple or large pills
  - Coping with side effects

The most challenging cases tend to be those where diagnosis and treatment of HIV and opportunistic infections have been delayed, and compliance with preventive medications has been poor.

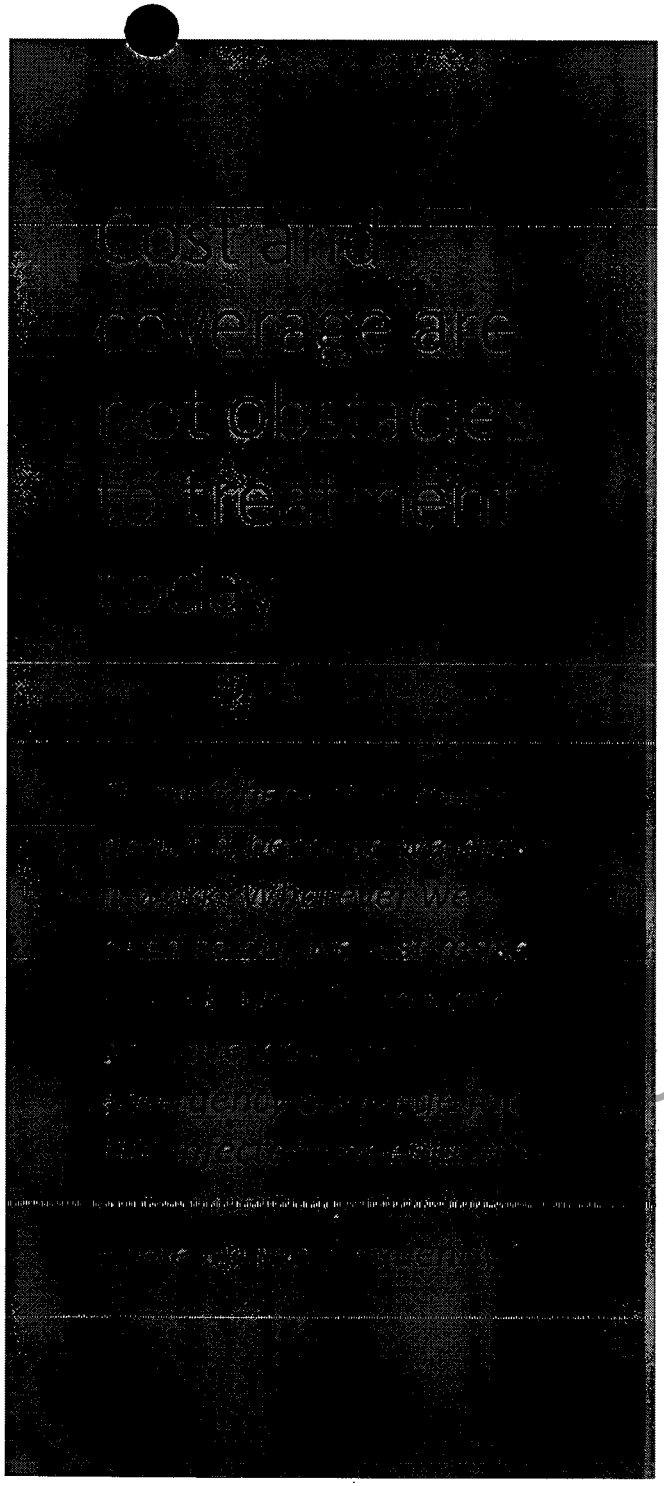
These factors may be compounded by a history of substance abuse and other psychosocial problems and poor socioeconomic circumstances.

For these patients in particular, strategies to support compliance and adherence are critical.

"It's highly diverse, but when patients have toxo, they're usually tougher patients where they're late to care. Sometimes they're suffering from housing needs. Sometimes they're suffering from mental health or substance abuse."

COST CHALLENGES AND TRADE-OFFS

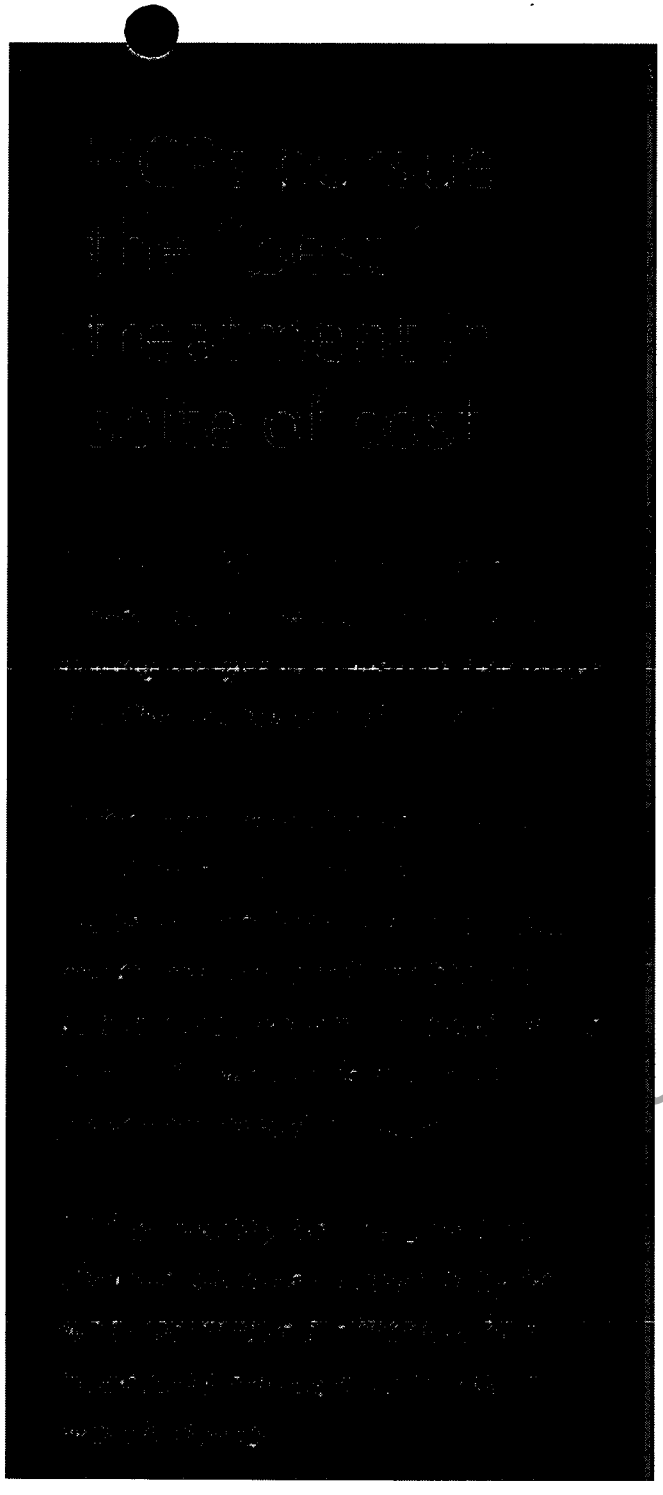
TURING
PHARMACEUTICALS



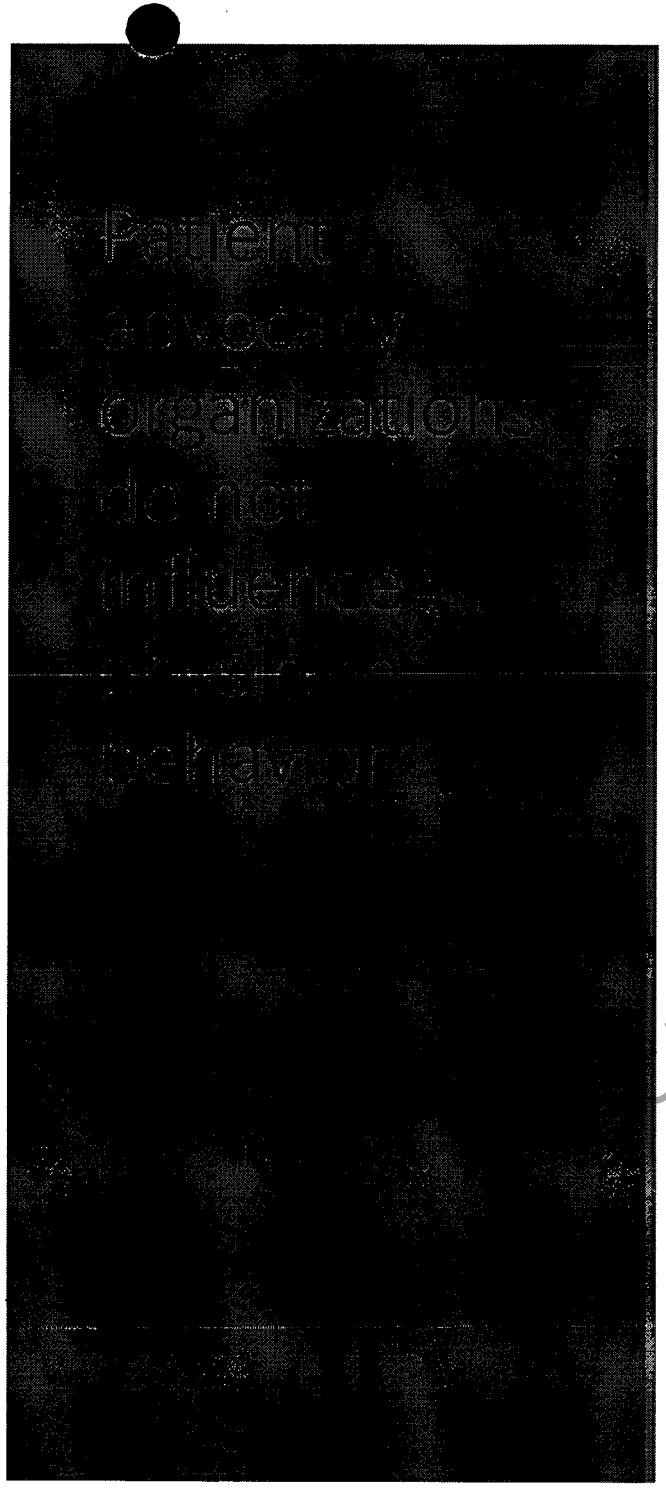
- Physicians do not report high out-of-pocket costs, required prior authorizations, or other access barriers to toxo medications
- The standard toxo treatments are perceived to be affordable but sulfa is thought to be relatively expensive, and Bactrim is inexpensive

For Medicaid beneficiaries, toxo drugs may be free

- The Kaiser Family Foundation reports that Medicaid covers half of all people with HIV in the country (March 2013)
- In this study, physician estimates for their patients covered by Medicaid range from <10% to 70
- ADAP coverage mentioned as well



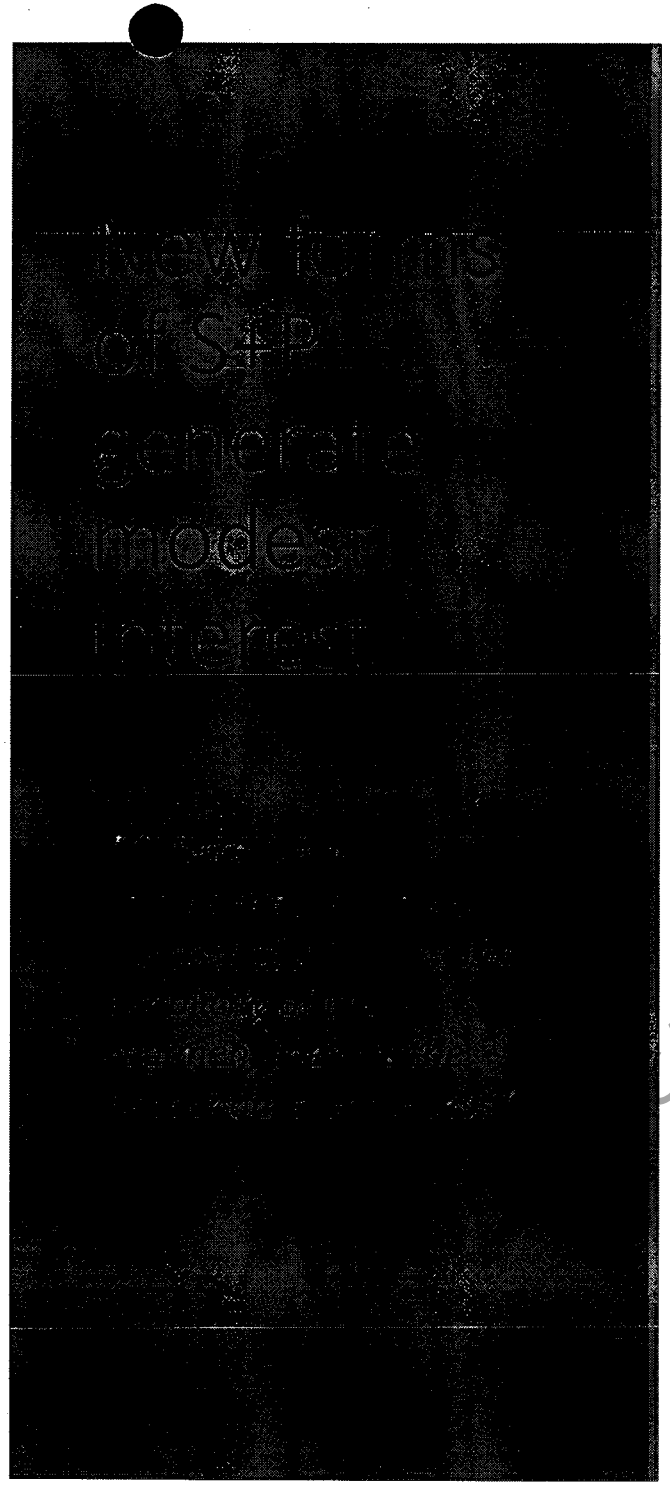
- Physicians would prefer not to have to substitute another drug for S or P and would complete prior authorizations or pursue financial support in the interest of securing "gold standard" treatment
  - Some would press patients to accept a higher cost in the interest of the best care
  - Some would explain the potential risk of a compromised outcome, especially in cases of severe neurological impairment
- If patients were to decline the "best" therapy due to cost, physicians would reluctantly prescribe their second line alternative to S
  - Some would expect and accept decreased efficacy, as suboptimal therapy would be better than no therapy
  - A few admitted that they "wouldn't lose sleep" over having to make the substitution
- Physicians are at a loss to think of an appropriate alternative to P
  - Second line regimens are based on P, the "backbone" of therapy
  - Might consult the literature or experts
  - A few mention atovaquone and Bactrim as possible substitutes



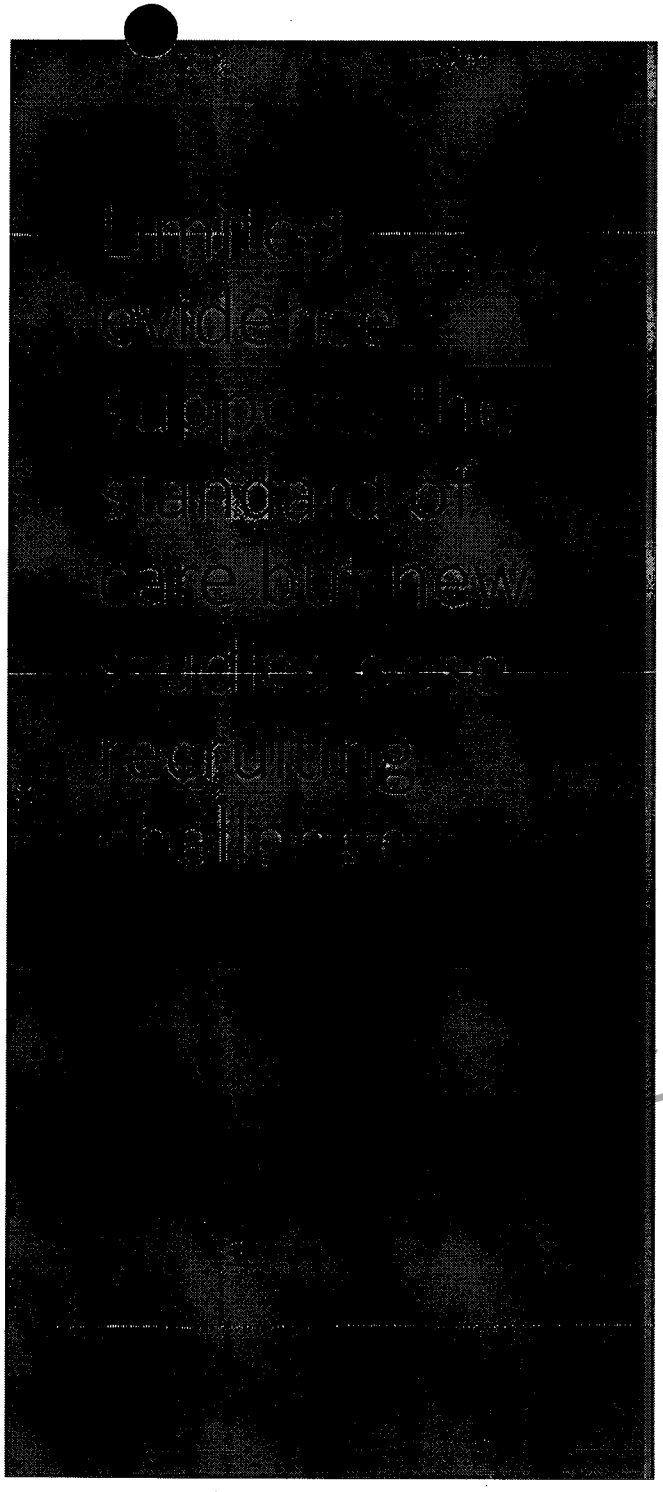
- Although they may be peripherally aware of lobbying and public relations initiatives, physicians are not themselves directly involved with patient advocacy organizations
  - More likely to participate in advocacy via their own professional societies
- In cases where they disprove of industry or individual manufacturers, physicians continue to pursue the "best" therapeutic option for patients, especially in potentially life-threatening situations
- Many feel the number of toxoplasmosis patients is too small to stimulate a significant lobbying effort were the cost of therapy to become an issue

OPPORTUNITIES AND UNMET NEEDS

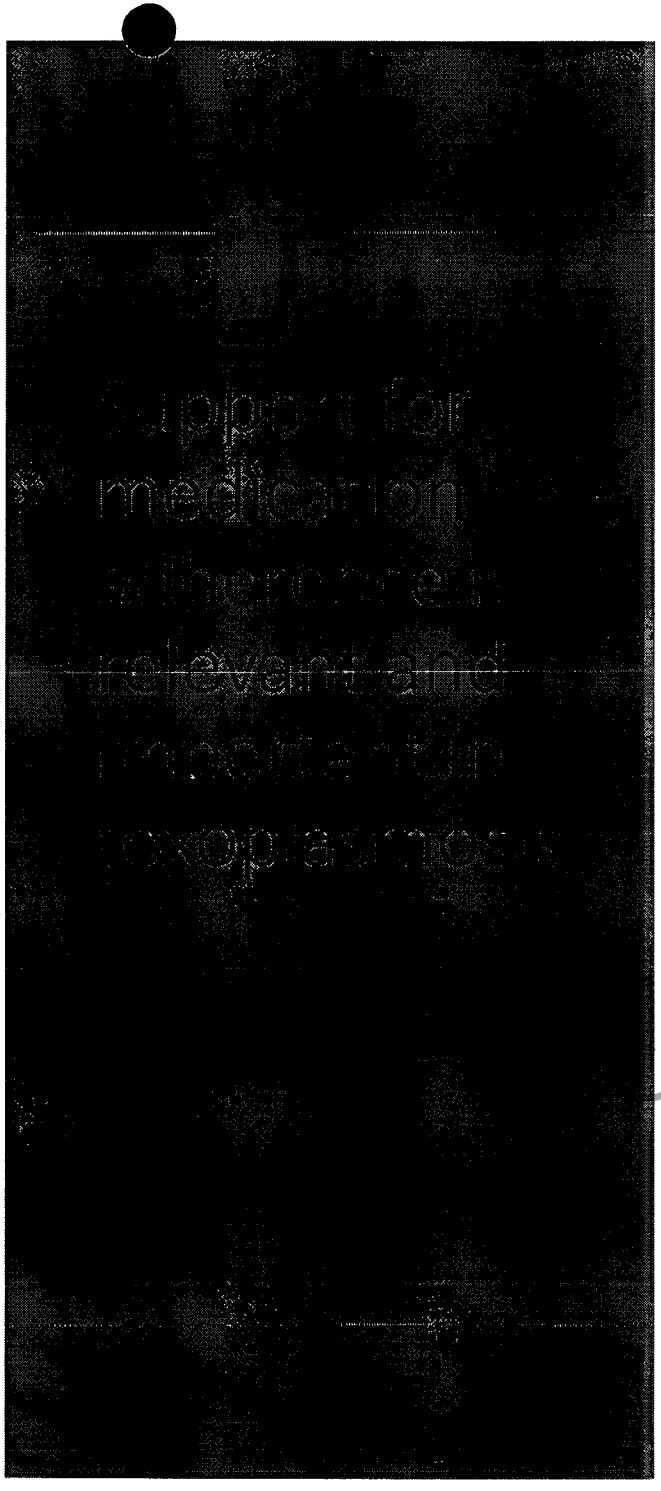
TURING
PHARMACEUTICALS



- Potential new formulations of S and P are a "no brainer" to improve compliance and adherence but are not a factor in whether the drugs will be used or used more
  - Multiple fixed dose combinations of S + P would be required to support acute versus maintenance dosages and differences in the recommended dosing frequency of each
    - A combination pill can't be too large
    - One recommendation: Sulfa 2000 mg/pyrim 25 mg BID and sulfa 1000 mg/pyrim 12.5 mg BID
- While P and Bactrim are both available in IV formulations for inpatient use, sulfadiazine is not which could be useful for NPO patients
- Extended release forms of drugs may also support adherence, *e.g.* an injectable formulation that is active for 1-3 months
- Packaging S and P together may also help patients, e.g. blister packs that make the regimen visually obvious and convenient



- Level I evidence regarding treatment of toxo is lacking and there may be opportunities to expand what is known about:
  - CNS-related outcomes
  - Quality of life
  - Survival
- Head-to-head studies are of interest but it would be extremely difficult to enroll appropriate populations in numbers sufficient for randomized control trials
  - Interest in a non-inferiority trial of S+P versus Bactrim: can a less expensive therapy be substituted for the standard of care?



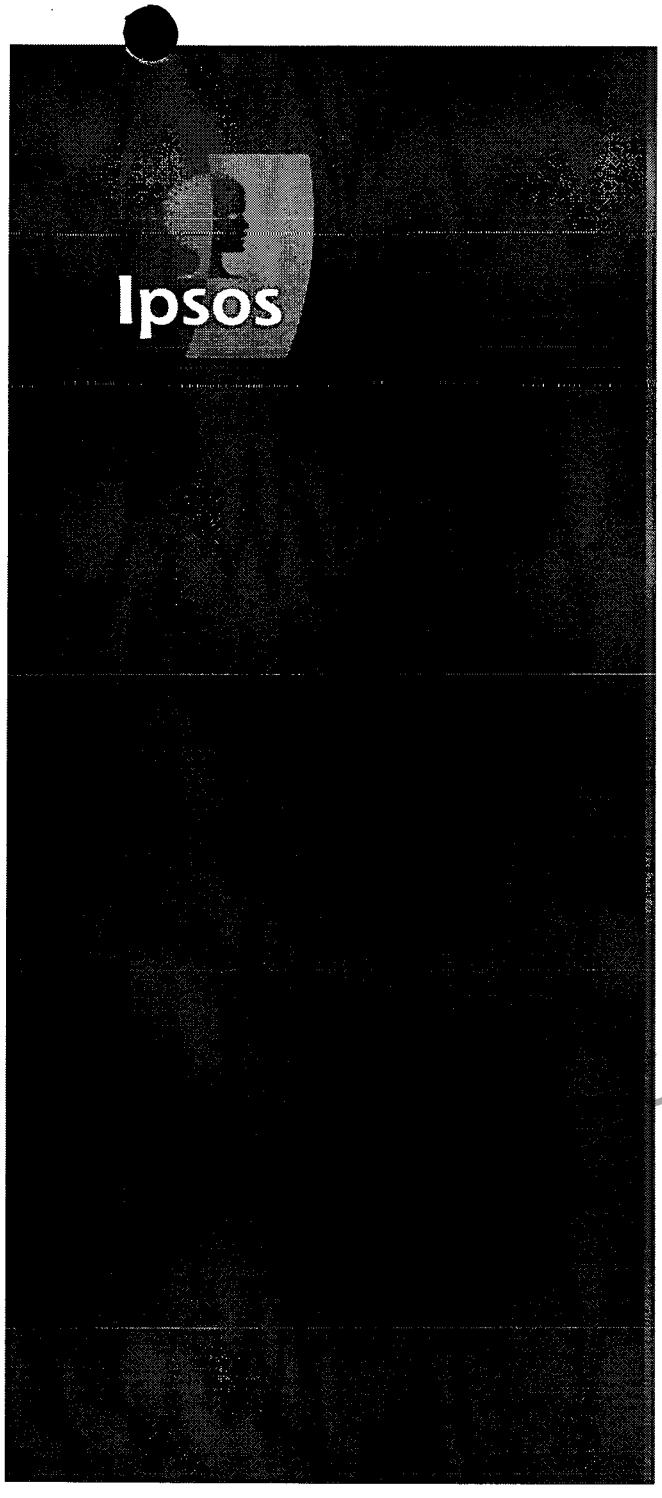
- Seriously ill patients being discharged from hospital or treated on an outpatient basis often have access to support
  - *E.g.* transportation services, home-based care, an assigned case worker/social worker, Medication Therapy Management services, etc.
- Additional resources to support medication adherence specifically could be useful, especially those that utilize technology:
  - Text-based medication reminders
  - Chip/reader attached to bottle cap to track and monitor compliance
  - Inbound and outbound telephonic support to patients (focused on adherence and managing side effects)
  - Visual aids to educate and remind about the treatment regimen
  - Support groups

APPENDIX

TURING
PHARMACEUTICALS

Screener

Discussion Guide



From: Nancy Retzlaff
To: Patrick Crutcher
CC: Martin Shkreli; Michael Smith; Tina Ghorban
Sent: 6/1/2015 8:34:09 AM
Subject: Re: trimethoprim

Patient services to support adherence of the Toxo regimen is a good opportunity to add value. Co pay assistance will also be important for adherence and ensuring the Rx gets filled without disruption for the physician.

Sent from my iPhone

On May 31, 2015, at 12:53 PM, Patrick Crutcher [redacted]> wrote:

Agree. Doc calls mostly indicated the same.

I remember another idea we had was co-pay assist on their *HIV* meds, since their lack of adherence there is why they end up with TE.

From: Martin Shkreli
Sent: Sunday, May 31, 2015 12:25 PM
To: Patrick Crutcher; Michael Smith
Cc: Nancy Retzlaff; Tina Ghorban
Subject: RE: trimethoprim

Good points on both. The other one Nancy has mentioned is if they've ever used trimethoprim prophylactically they will want a different therapy for treatment.

Also pyrimethamine has a much better logP (2.69) vs trimethoprim (0.91). It gets into the brain easily while trimethoprim has some issues. There are no real studies for trimethoprim. But the idea that you could use trimethoprim+sulfa or trimethoprim+clinda (and of course just Bactrim), is clearly the biggest worry. Most docs and insurers will not want to mess around and with our sales force pounding these messages home, we might even be able to grow units, especially while our reimbursement specialists are fielding any cost concerns.

From: Patrick Crutcher
Sent: Sunday, May 31, 2015 12:20 PM
To: Michael Smith; Martin Shkreli
Cc: Nancy Retzlaff; Tina Ghorban
Subject: Re: trimethoprim

To play devil's advocate - with respect to Bactrim, could it come down to a physicians experience level with either agent? Have they had the same experience as the Italian or West French Indies studies(papers attached)? Are they comfortable deviating from the guidelines?

?HIV guidelines for toxoplasmosis

https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/322/toxo

From: Michael Smith
Sent: Sunday, May 31, 2015 10:09 AM
To: Martin Shkreli; Patrick Crutcher
Cc: Nancy Retzlaff; Tina Ghorban
Subject: Re: trimethoprim

Not much other than it's not labeled for toxo. Also, I would think docs would go for bactrim first if they were looking for alternative therapies. They'd have to use tmp with sulfadiazine, since sulfamethoxazole isn't available as an individual rx. TMP-SMX is a better characterized therapy than tmp-sulfadiazine, so docs would be blazing new ground, in a way.

----- Reply message -----
From: "Martin Shkreli" [redacted] "Michael Smith" [redacted]
Cc: "Nancy Retzlaff" [redacted] "Tina Ghorban" [redacted]
Subject: trimethoprim
Date: Sat, May 30, 2015 11:45 PM

Is available for Rx by itself. What is to stop someone from using that instead of pyrimethamine?

MS

From: Tina Ghorban
To: Stephanie Brown
Sent: 6/1/2015 9:41:20 AM
Subject: FW: Development in Toxo....Still a while out though

My initial comment and Nancy's response

From: Nancy Retzlaff
Sent: Friday, May 22, 2015 6:20 AM
To: Tina Ghorban
Cc: Michael Smith; Patrick Crutcher
Subject: Re: Development in Toxo....Still a while out though

Thanks Tina.

Based on the interviews I heard, I'm not sure I completely agree with the blanket statement that "Bactrim is being used or would be used without issue or sacrifice in care". I heard quite consistently a more emotional response top of mind e.g. "I would feel uncomfortable", willingness to challenge an insurance company for access and the desire to have non-inferiority data. Last night the physician said he would call the manufacturer if need be to get assistance with payment. I agree when pressed they try to rationalize substitution, but the initial emotional response suggests an opportunity to influence and fuel the doubt.

My sense is that if the patient declined to accept the treatment due to a high co-pay then that would force substitution and build experience. We want to avoid that situation. The need to address co-pay assistance is a key success factor.

If I assess their responses from the perspective of trying to market or sell Bactrim as an appropriate substitution I think the hurdles would be quite high.

Given the fragile nature of these patients and history of non-adherence, there seems to be perceived value in offering high touch service and patient support.

But I'm a marketing optimist!

Nancy

On May 21, 2015, at 10:46 PM, Tina Ghorban [redacted]> wrote:
Ah, thanks. Good to know.

Here are my notes with some key high-level themes:

* ID is almost always treater for toxo. Acute treatment is started in hospital in severe cases, often severe with HIV patients.

* Guidelines are more important for toxo because field is not changing- fewer opportunistic infections, so there are no new products or research.

* Guidelines and experience favor S+P combination, but Bactrim use and use of other agents definitely occurring without much issue or sacrifice in care.

* Bactrim used 1L by some HCPs already. Younger IMs may prefer Bactrim due to concerns about kidney stones/renal toxicity with sulfadiazine, and ease of access and low cost, particularly in hospital setting.

* Pyrimethamine seems to be considered more the "backbone" of treatment vs sulfadiazine. HCPs more willing to swap out sulfa and replace with clindamycin or dapsone or atovaquone in conjunction with pyrimethamine.

* Priority in treatment is for patients to actually take medicines, so willing to sacrifice "best" therapy for therapy that patient can tolerate and afford

* Challenge to treatment success is compliance, particularly with HIV patients. These are the "train wreck" patients...confounding social, emotional and financial issues that make consistent treatment difficult. "Compliance is not an issue...except for those where compliance is always an issue"

* Possible lifecycle opportunities: fixed-dose combination (careful of pill size), extended release tablets to reduce overall pill burden, IV formulations, additional data to support use in other common OI's such as pneumocystis
Please remember that this is blinded research, so we just record their responses and don't correct or challenge them on their beliefs; we only probe on rationale or to clarify. Perception is reality for most people, so we need to know what they believe today in order to identify how much work it will take to get them to make a decision or take a specific action, i.e. prescribe our product.

Let me know if you have any questions.
Tina

- receipt of all necessary consents from any governmental authorities or creditors, lessors or customers of the Seller.

Due Diligence:	The Seller shall provide to the Purchaser, including its directors, officers, employees, agents, lenders, investors, funding sources, counsel, accountants, consultants or advisors, complete access to all of the Seller's books, records, premises, personnel, customers and suppliers with respect to the Assets.
Representations, Warranties and Covenants:	The Purchaser and the Seller will make standard representations, warranties and covenants typically associated with transaction of this nature.
Fees:	Each party will pay their respective fees, costs and expenses incidental to the completion of the transactions contemplated by this Term Sheet.
Confidentiality:	Until the closing of the transactions contemplated by this Term Sheet, the existence and terms of this Term Sheet and the fact that negotiations may be ongoing with the Purchaser shall not be disclosed to any third party without the consent of the Purchaser, except as may be (i) reasonably required to consummate the transactions contemplated hereby (*provided* that any persons receiving the information agree to the confidentiality restrictions contained herein or are otherwise subject to confidentiality obligations) or (ii) required by law.
Good Faith Negotiations:	The Purchaser and the Seller agree to negotiate diligently and in good faith to prepare and execute the documentation contemplated by this Term Sheet as soon as practicable.
Governing Law and Forum:	New York. Any disputes relating to the transactions contemplated hereby shall be heard in the State and Federal courts located in the County of New York in the State of New York.

TURING

PHARMACEUTICALS

Assessing The Market Potential For Sulfadiazine And Pyrimethamine

June 10, 2015

Table of Contents

Objectives and Methodology

Business Objective:

- Evaluate the potential to preserve the value of sulfadiazine and/or pyrimethamine for the treatment of toxoplasmosis in the event of an increase in the cost of these agents.

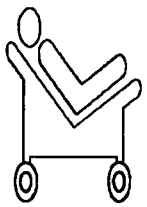
Research Objectives:

- Clarify the toxoplasmosis treatment algorithm and considerations in selecting therapies
- Identify differences in approach for specific patient sub-populations
- Determine the impact of cost on treatment decisions by sub-population
- Explore opportunities to enhance the value of sulfadiazine and/or pyrimethamine in the treatment of toxoplasmosis, *e.g.* lifecycle strategies and partnerships

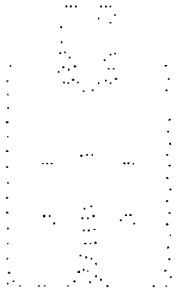
Physician Telephone Depth Interviews - May 20, 21, 22, 2015					
Infectious Disease	Pediatric Infectious Disease	PCP's	Internal Medicine	OB/GYN	TOTAL
7	1	2	5	2	17

Executive Summary

Toxoplasmosis Treatment Context

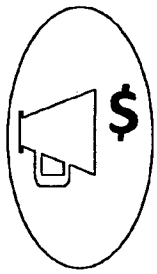


Mostly seen in HIV patients who are often non-compliant; may wait until treatment is critical



Typically present to hospital ER and are admitte

All patients referred to Infectious Disease (ID) specialist



IDs will advocate for the standard of care, even if it's costly

Non-compliance is the largest barrier to treatment

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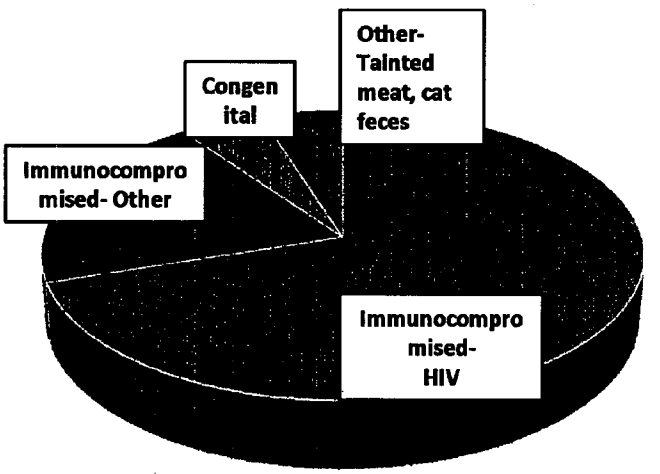
The Patient

- **Most are HIV positive**
- **May lack medical care**
- **Often non-compliant**
- **Limited resources to pay**
- **Need urgent treatment**

- The majority of toxoplasmosis (toxo) cases are seen in HIV-infected patients. In many cases, these are patients who:
  - Have not sought regular medical care with the result that diagnosis and treatment of HIV and opportunistic infections may have been delayed
  - Struggle to comply with long-term and/or complex preventive medication regimens
  - Have limited ability to pay for treatment
- Incidence is perceived to be decreasing as improved HIV treatments have resulted in relatively stable immunity today
- The need to treat is considered urgent in all types of cases with the goal of stabilizing disease, not eradicating it, and treatment is often initiated in-hospital



The Doctor

- **Infectious Disease specialist**
- **Limited evidence available to guide care**

- Treatment is commonly initiated by infectious disease specialists (IDs)
- Poor clinical evidence is available to guide treatment of toxo; most physicians reference CDC, NIH and IDSA guidelines for managing toxo in HIV patients, expert opinion, and personal experience
  - With fewer opportunistic infections in the population, newer treatments are not being developed, and guidelines have not been updated or amended to address non-HIV populations

The Treatment

- **S and P first line of defense**
- **Bactrim is an alternative for a small subset of physicians**
- **Clindamycin is a substitute for S for sulfa allergies**
- **P tolerability is good - the 'backbone' of therapy**
- **Bactrim for maintenance**

- Regardless of the treatment setting, nearly all physicians prescribe sulfadiazine (S) and pyrimethamine (P) first line for all types of toxo cases
  - Response is often seen in 2-3 weeks
  - For HIV patients, acute treatment usually lasts 3-6 weeks
  - Bactrim is an alternative first line treatment for a very small subset of physicians who may tend to be younger and prefer the simplicity and cost advantages of a combination pill
- Clindamycin is the primary substitute for S in patients exhibiting a sulfa allergy
- P tolerability is good, and side effects are rarely observed; thus it is a "backbone" of therapy and not often substituted
- Bactrim is preferred for prophylaxis in HIV patients and as maintenance therapy in all patients who require it
  - Fixed dose combination supports compliance and is relatively inexpensive – both important for long-term use

Typical Toxoplasmosis Treatment Flow

1. Patient presents with acute symptoms (CNS abnormality, seizures, abnormality of gait) to ER or regular PCP/IM/ID

2.  Patient is admitted to the hospital in the care of an ID for brain imaging

3. ID Rx's S+P and possibly IV steroids
   - If sulfa allergy, substitute clinda
   - If clinda intolerable, substitute atoquavone, Dapsone, or Zithromax

4. Discharge on oral S+P, or possibly switch to Bactrim for cost and convenience

5. Acute treatment usually lasts for 3-6 weeks
   - If sulfa allergy, substitute clinda
   - If S+P not well reimbursed, substitute Bactrim

6. Bactrim for ongoing maintenance as necessary (for convenience, cost and protects against pneumocystis pneumonia and nocardia), usually until CD4 > 200 for > 6 months

The Cost

- **Cost and coverage are not currently obstacles to treatment**

COST CHALLENGES

- Physicians would prefer not to have to substitute another drug for S or P due to cost
- Most physicians would complete prior authorizations or pursue financial support in the interest of securing "gold standard" treatment for patients

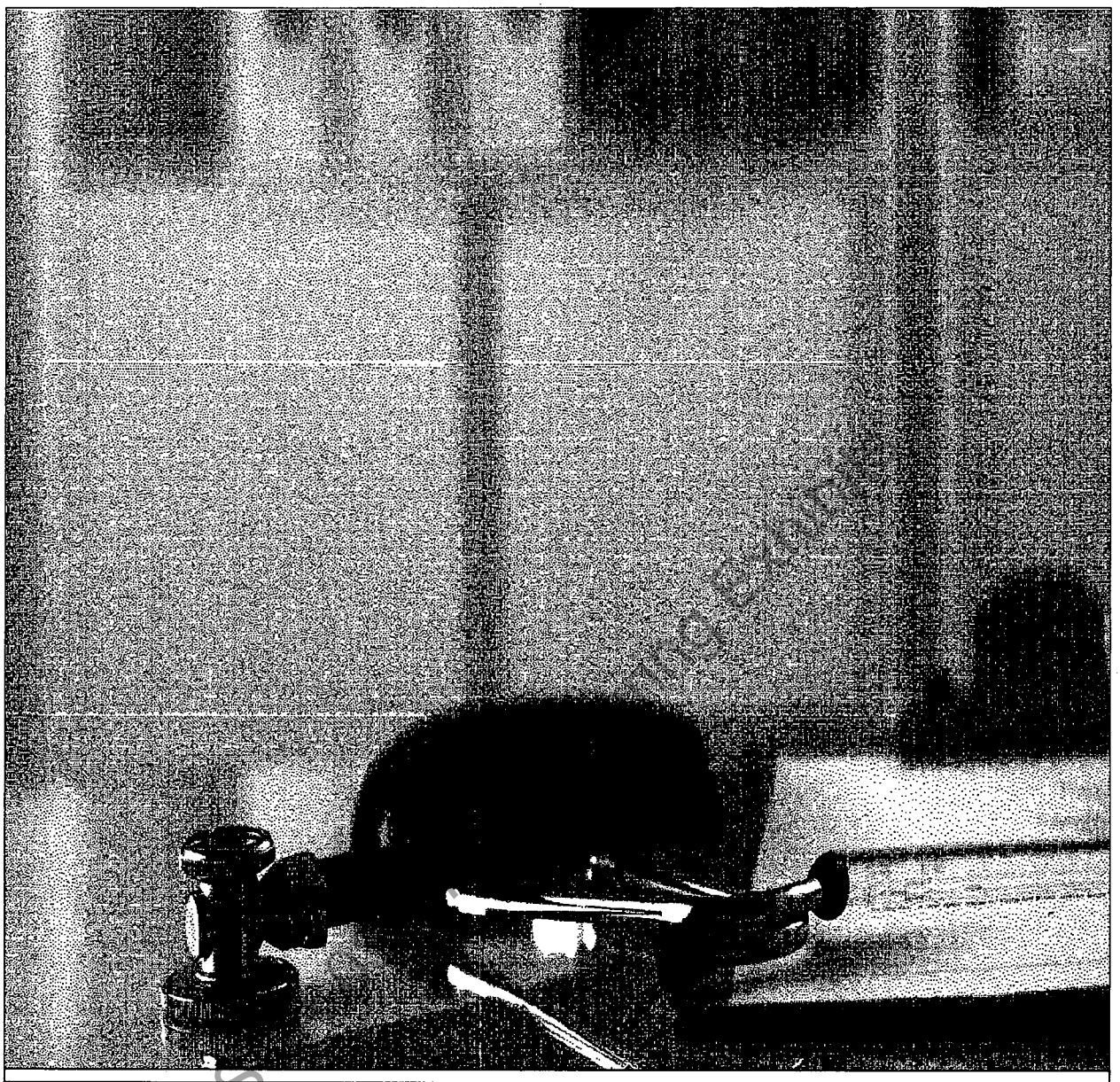
TRADE-OFFS

- If patients were to decline the "best" therapy due to cost, physicians would reluctantly prescribe their 2L alternative to S
  - Would expect and be resigned to decreased efficacy
  - Sub-optimal therapy would be considered better than no therapy
- Physicians are at a loss to think of an appropriate alternative to P

The Opportunity

- **Compliance and adherence are the biggest barriers to effective treatment**
- **New formulations could address unmet needs**
- **Adding to the body of clinical evidence also helpful**

- Fixed dose combinations of S and P are a *"no brainer"* to help improve compliance
  - Multiple combinations would be required for acute versus maintenance dosages and to accommodate differences in the recommended dosing frequency of each
  - Pill size may be an issue
  - Extended release formulations (*e.g.*, one injection per month) would also address compliance issues
- S and P in an IV formulation could be useful for NPO patients in-hospital
- Resources/services to support medication adherence could be useful, especially those that utilize technology, *e.g.* a digital monitoring device on pill bottle cap
- New Level I evidence about optimal treatment of toxo is needed, especially head-to-head studies, but it may be extremely difficult to enroll appropriate populations in numbers sufficient for randomized control trials



Conclusions and Recommendations

Cost Perception

Conclusion

As the clinicians primarily responsible for toxo treatment, IDs are not cost- or price-sensitive

- Highly focused on therapeutic benefit
- Think current cost of pyrimethamine + sulfadiazine is more expensive than other 2L therapies already but consider it the gold standard nonetheless
- Will take action to secure "best" treatment for patients

Recommendation

Enhance the S+P value proposition and offset perceptions of high cost

- Make the regimen affordable with a Patient Assistance Program for patients unable to pay

Patient Needs

Conclusion

Patient compliance is the biggest obstacle to effective treatment

- Compliance with a complicated regimen
- Adherence over a long period, possibly a lifetime
- Long-term out-of-pocket expense

Recommendation

Make the regimen easier for compliance

- Medication reminder platform
- New formulations and packaging, *e.g.* combination pills, extended release formulations, combination blister packs, IV formulations, etc.

Support for the Standard of Care

Conclusion

Although current guidelines are clear, evidence supporting S+P is limited

- Currently limited to HIV primarily
- All physicians, and IDs in particular, value clinical data and would be receptive to new information

Recommendation

Deepen ID commitment to the standard of care

- Invest in a retrospective analysis of cases or an expert panel review regarding toxo treatment and outcomes in HIV and other affected populations

Payer Strategy

Conclusion

Commercial and public payers do not appear to scrutinize pricing of toxo drugs today

- Low incidence disease
- Out-of-pocket burden is not an obstacle for most patients, despite payer ability to cost-shift or eliminate access altogether

Recommendation

Formulate and implement a payer strategy

- Conduct market research among commercial payers to assess the potential impact of various pricing scenarios
- Consult experts to understand Medicaid pricing and the impact of price increases

Detailed Findings

TREATMENT ENVIRONMENT

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Incidence is decreasing but treating toxoplasmosis is an urgent matter

"It's challenging because it's not only one thing, the parasite. It's also the immune response. And each person is different. So you have a factor here you can't really control and standardize between patients: the host response to the parasite. That makes it very complicated."

- The vast majority of toxoplasmosis cases are seen in HIV-infected patients, followed by (in order of frequency of mentions):
  - Other immunocompromised patients such as transplant patients and patients on chemotherapy
  - Retinitis
  - Immunocompetent patients
  - Congenital
  - Pregnancy
- Incidence is perceived to be decreasing as improved antiretroviral therapy and widespread use of Bactrim as prophylaxis (in HIV patients with CD4 counts <200) result in relatively stable immunity today
- The need to treat is considered urgent in all types of cases, and treatment is often initiated in-hospital
- Goals of treatment are stability and control, not eradication, as disease often recurs

Infectious Disease specialists lead treatment and the clinical team

- Patients experiencing serious symptoms may present in the ER or be immediately recommended for admission by their outpatient physician
- PCPs, IMs, and ob/gyns typically refer to an infectious disease specialist (ID) when a diagnosis is suspected or confirmed via imaging studies, PCR testing, or IgG and IgM testing
- Treatment is most commonly initiated by infectious disease specialists (IDs) in both the inpatient and outpatient settings
  - Other physicians may be involved in co-management and monitoring, especially during the maintenance phase of therapy

Sulfadiazine and pyrimethamine are the first line standard for acute care

"There hasn't been a tremendous amount of new data because we've had a smaller number of cases with the reduction in opportunistic infections. They haven't updated these guidelines recently. So we're sort of stuck with the older experience."

- Regardless of the treatment setting, nearly all physicians prescribe sulfadiazine and pyrimethamine for all acute patients
  - Consistent with CDC and NIH guidelines for managing toxo in HIV patients which are generalized to other populations
  - Bactrim is an alternative first line treatment for a very small subset of physicians who may tend to be younger and prefer the simplicity and cost advantages of a combination pill
  - Leucovorin is used concomitantly in HIV patients
  - Although not commercially available in the U.S., spiramycin is recommended for infected women <18 weeks into their pregnancy, and S+P is recommended for infected women >18 weeks into their pregnancy
  - For congenital cases, S+P or Bactrim may be used
- Many perceive S+P to offer efficacy superior to other options but physicians acknowledge limited Level I evidence is available
- Perception is that sulfadiazine may be delivered intravenously to inpatients (although an IV formulation is not commercially available); patients are discharged with prescriptions for oral S+P
- Patients are typically treated with S+P for 3-6 weeks, when symptoms may be lessened or resolved and/or imaging reveals brain and/or eye lesions have shrunk in size

Clindamycin dominates 2L treatment after sulfadiazine but some use other options

- For patients exhibiting a sulfa allergy or side effects, clindamycin is the primary second line treatment substituted for sulfadiazine
  - Although clinical evidence is poor, clinda thought to offer efficacy inferior to sulfadiazine despite patients progressing well on it
- Pyrimethamine is generally well-tolerated, and substitutions do not appear to be necessary
- Second or third line alternatives to S, especially in those who don't tolerate clinda or do not respond to treatment, include:
  - Atoquavone
  - Dapsone
  - Zithromax
  - Possibly high dose Bactrim

Bactrim owns maintenance treatment and prophylactic therapy

"While we would like to follow guidelines and be able to give them the best care possible, sometimes it needs compromising the gold standard treatment with something you think is going to be more tolerable, namely monotherapy for simplicity."

- After the acute phase of toxo treatment, HIV patients are routinely transitioned to Bactrim for maintenance, sometimes even before full treatment regimen of S+P is complete
  - Convenient combination regimen is inexpensive and straightforward relative to S+P
  - Broad spectrum antibiotic protects against other opportunistic infections
  - HIV patients will continue until CD4 counts are >200 for at least six months and possibly for a lifetime
- Post-acute therapy for non-HIV patients is lower doses of S+P or therapy may be discontinued depending on clinical and radiologic evidence of remission/ongoing disease
- Bactrim is commonly used as prophylactic therapy to prevent pneumocystis pneumonia in HIV patients with CD4 counts < 200
  - Prevention of toxo is a side benefit; *"two birds with one stone"*

Adherence is the biggest obstacle to effective treatment

"Compliance is never an issue....except for those in whom compliance is always an issue."

"Human ability to take a complicated pill regimen is very challenging especially since the people who end up in this position are the ones who weren't taking pills in the first place. So it's only that that stands in the way."

- S+P comprises a difficult regimen, especially for HIV patients taking multiple medications.
- "Medication exhaustion" stems from:
  - A frequent and complicated dosing regimen
    - S is QID, P is TID
  - Difficulty swallowing multiple or large pills
  - Coping with side effect

The most challenging cases tend to be those where diagnosis and treatment of HIV and opportunistic infections have been delayed, and compliance with preventive medications has been poor.

These factors may be compounded by a history of substance abuse and other psychosocial problems and poor socioeconomic circumstances.

For these patients in particular, strategies to support compliance and adherence are critical.

"It's highly diverse, but when patients have toxo, they're usually tougher patients where they're late to care. Sometimes they're suffering from housing needs. Sometimes they're suffering from mental health or substance

COST CHALLENGES AND TRADE-OFFS

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Cost and coverage are not obstacles to treatment today

"I don't hear that much about it because we make it work. Whatever we need to do, we just make it work. Usually this can get covered under emergency coverage for HIV infected patients. It's not something that has come up too frequently."

- Physicians do not report high out-of-pocket costs, required prior authorizations, or other access barriers to toxo medications
- The standard toxo treatments are perceived to be affordable but sulfa is thought to be relatively expensive, and Bactrim is inexpensive

For Medicaid beneficiaries, toxo drugs may be free

- The Kaiser Family Foundation reports that Medicaid covers half of all people with HIV in the country (March 2013)
- In this study, physician estimates for their patients covered by Medicaid range from <10% to 70
- ADAP coverage mentioned as well

HCPs pursue the "best" treatment in spite of cost

"Unless they just plain are not covering it, I would just keep trying to get it covered because it's the standard of care."

"Theoretically the second or third line mechanism is very close to the first line. It would make me uncomfortable [to substitute] based on experience but still I would feel this is probably good enough."

"I'd probably be resigned to choose an alternative maybe with decreased efficacy, but hopefully enough to make it

- Physicians would prefer not to have to substitute another drug for S or P and would complete prior authorizations or pursue financial support in the interest of securing "gold standard" treatment
  - Some would press patients to accept a higher cost in the interest of the best care
  - Some would explain the potential risk of a compromised outcome, especially in cases of severe neurological impairment
- If patients were to decline the "best" therapy due to cost, physicians would reluctantly prescribe their second line alternative to S
  - Some would expect and accept decreased efficacy, as suboptimal therapy would be better than no therapy
  - A few admitted that they "wouldn't lose sleep" over having to make the substitution
- Physicians are at a loss to think of an appropriate alternative to P
  - Second line regimens are based on P, the "backbone" of therapy
  - Might consult the literature or experts
  - A few mention atovaquone and Bactrim as possible substitutes

Patient advocacy organizations do not influence physician behavior

- Although they may be peripherally aware of lobbying and public relations initiatives, physicians are not themselves directly involved with patient advocacy organizations
  - More likely to participate in advocacy via their own professional societies
- In cases where they disprove of industry or individual manufacturers, physicians continue to pursue the "best" therapeutic option for patients, especially in potentially life-threatening situations
- Many feel the number of toxoplasmosis patients is too small to stimulate a significant lobbying effort were the cost of therapy to become an issue

OPPORTUNITIES AND UNMET NEEDS

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New forms of S+P generate modest interest

"If there is a way to reduce the frequency, number of pills, and the simplicity of the regimen, there is the best chance of success."

- Potential new formulations of S and P are a "no brainer" to improve compliance and adherence but are not a factor in whether the drugs will be used or used more
  - Multiple fixed dose combinations of S + P would be required to support acute versus maintenance dosages and differences in the recommended dosing frequency of each
    - A combination pill can't be too large
    - One recommendation: Sulfa 2000 mg/pyrim 25 mg BID and sulfa 1000 mg/pyrim 12.5 mg BID
- While P and Bactrim are both available in IV formulations for inpatient use, sulfadiazine is not which could be useful for NPO patients
- Extended release forms of drugs may also support adherence, *e.g.* an injectable formulation that is active for 1-3 months
- Packaging S and P together may also help patients, e.g. blister packs that make the regimen visually obvious and convenient

Limited evidence supports the standard of care but new studies pose recruiting challenge

- Level I evidence regarding treatment of toxo is lacking and there may be opportunities to expand what is known about:
  - CNS-related outcomes
  - Quality of life
  - Survival
- Head-to-head studies are of interest but it would be extremely difficult to enroll appropriate populations in numbers sufficient for randomized control trials
  - Interest in a non-inferiority trial of S+P versus Bactrim: can a less expensive therapy be substituted for the standard of care?

Support for medication adherence is relevant and important in toxoplasmosis

- Seriously ill patients being discharged from hospital or treated on an outpatient basis often have access to support
  - *E.g.* transportation services, home-based care, an assigned case worker/social worker, Medication Therapy Management services, etc.
- Additional resources to support medication adherence specifically could be useful, especially those that utilize technology:
  - Text-based medication reminders
  - Chip/reader attached to bottle cap to track and monitor compliance
  - Inbound and outbound telephonic support to patients (focused on adherence and managing side effects)
  - Visual aids to educate and remind about the treatment regimen
  - Support groups

APPENDIX

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Screener cussion Gu

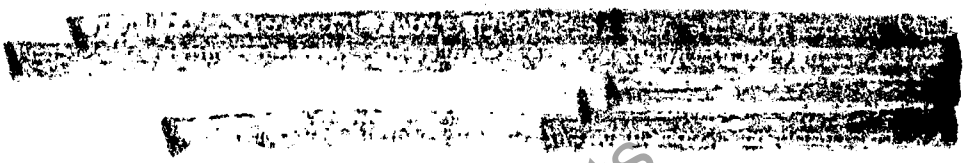
Ipsos

From:	Michael Smith
To:	Martin Shkreli
Sent:	6/10/2015 2:38:55 PM
Subject:	Data Room for Perceptive
Attachments:	Project Dart Data Room.pdf

I've attached it to this email

Michael Smith
Senior Director
Business Development

Turing Pharmaceuticals
[redacted]



Turing Pharmaceuticals Daraprim Diligence Questions

Diligence Requirements

1. Please provide historical net sales and units for 2012-2015
2. Please provide historical gross to net calculations for 2012-2015
3. Please provide the historical payer mix for 2012-2015
4. Our business intelligence has revealed that Mirror Pharmaceuticals filed an ANDA in 2014. Do you have any further information on this or any other ANDA(s) that may have been filed? Have any generics companies contacted Impax or Core Pharma to request product for bioequivalence testing?
5. How much inventory is currently in the channel?

Optional Questions

6. How much API inventory and finished goods inventory are currently on hand?
7. Please provide a brief overview of the supply chain for Daraprim
8. Are there any promotional efforts around Daraprim? What is the historical sales & marketing spend for Daraprim for 2012-2015?

Notes

Diligence Requirement #3: Please provide the historical payer mix for 2012-2015 - percent of sales for those years that are cash payers, third party commercial payers and government payers, including a breakdown between Medicare and Medicaid

Impax Response: Impax does not capture this information.

Diligence Requirement #4: Our business intelligence has revealed that Mirror Pharmaceuticals filed an ANDA in 2014. Do you have any further information on this or any other ANDA(s) that may have been filed? Have any generics companies contacted Impax or Core Pharma to request product for bioequivalence testing?

Impax Response: Impax does not have any knowledge of ANDA filers. Impax has not been contacted by any generic companies to request product for bioequivalence testing.

Optional Question #8: Are there any promotional efforts around Daraprim? What is the historical sales & marketing spend for Daraprim for 2012-2015?

Impax Response: No promotional [redacted] were spent

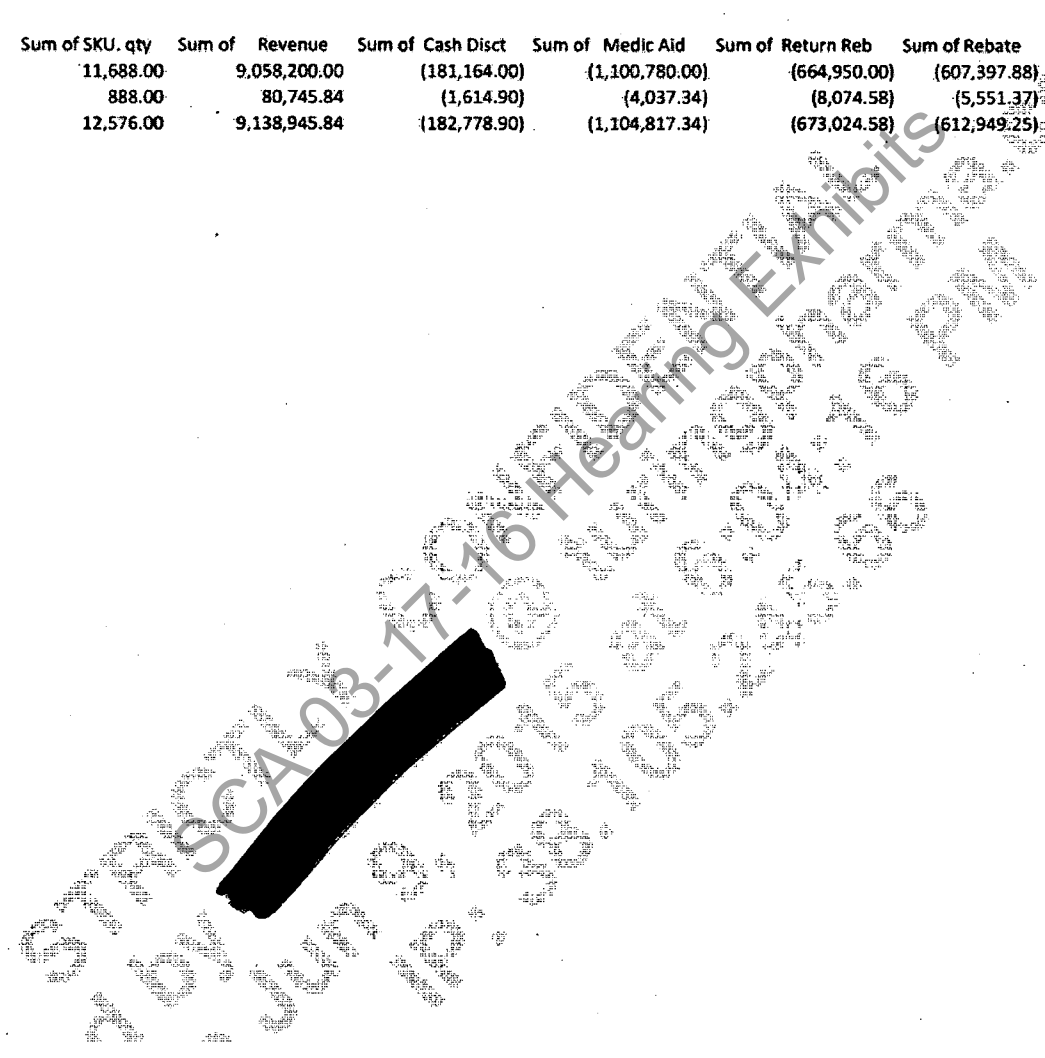
Daraprim				
Year	Unit	Sales $$	GP$$	GM%
2011	12,600	5,124,880	4,917,938	96.0%
2012	11,004	5,620,644	4,658,223	82.9%
2013	10,260	5,843,680	3,893,664	66.6%
2014	9,708	4,932,521	3,034,509	61.5%
2015-Q1	1,836	1,226,665	751,543	61.3%
2015-April	672	392,635	239,180	60.9%

Daraprim GTN Detail		
Year	Unit	Sales $$
2011	12,576	5,114,512
2012	11,004	5,620,644
2013	10,260	5,829,586
2014	9,708	4,932,521
2015-Q1	1,836	1,226,665
2015-April	672	392,635

Daraprim Inter		
Year	Unit	es $$
2011		10,368
2012		(0)
2013		14,094
2014		0
2015-Q1		-
2015-April		-

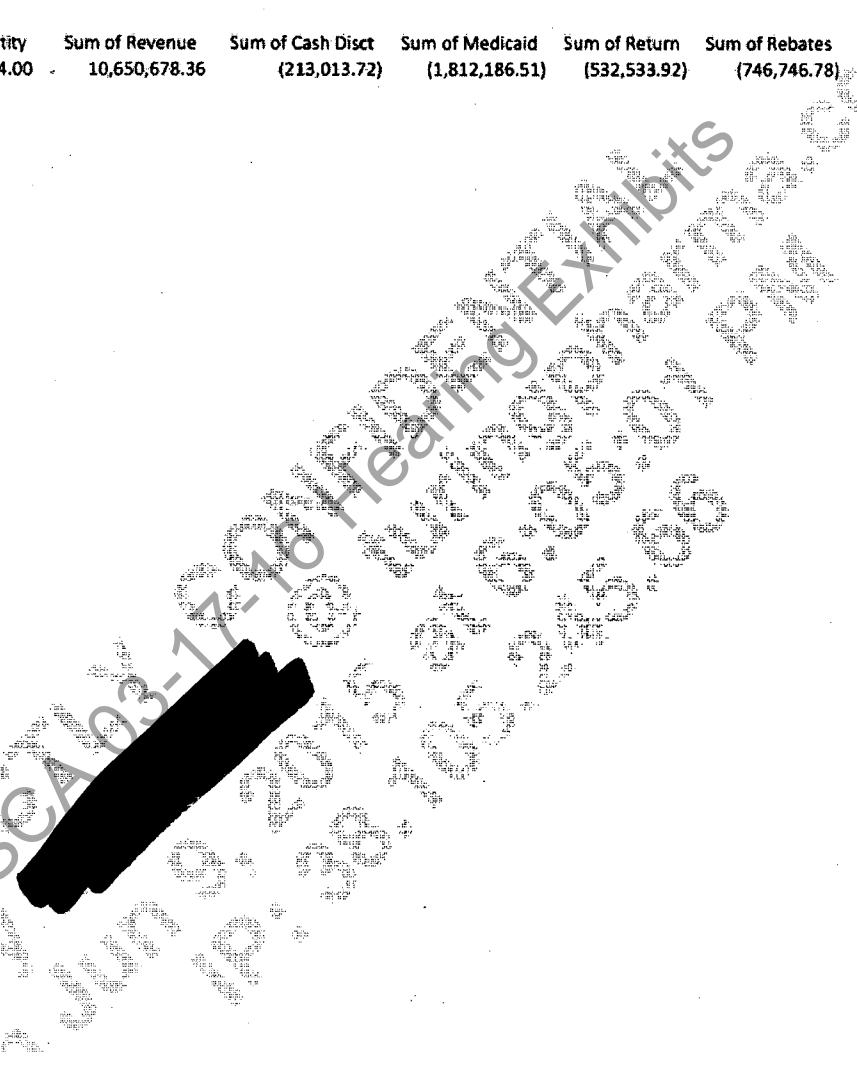
Gross to Net 2011

Row Labels	Sum of SKU. qty	Sum of Revenue	Sum of Cash Disct	Sum of Medic Aid	Sum of Return Reb	Sum of Rebate	Sum of Chargebacks	Sum of Net Sales
Daraprim 25 Mg 100 Ct	11,688.00	9,058,200.00	(181,164.00)	(1,100,780.00)	(664,950.00)	(607,397.88)	(1,445,487.72)	5,058,420.40
Daraprim Tabs 25mg 100ct GSK	888.00	80,745.84	(1,614.90)	(4,037.34)	(8,074.58)	(5,551.37)	(5,376.00)	56,091.65
Grand Total	12,576.00	9,138,945.84	(182,778.90)	(1,104,817.34)	(673,024.58)	(612,949.25)	(1,450,863.72)	5,114,512.05



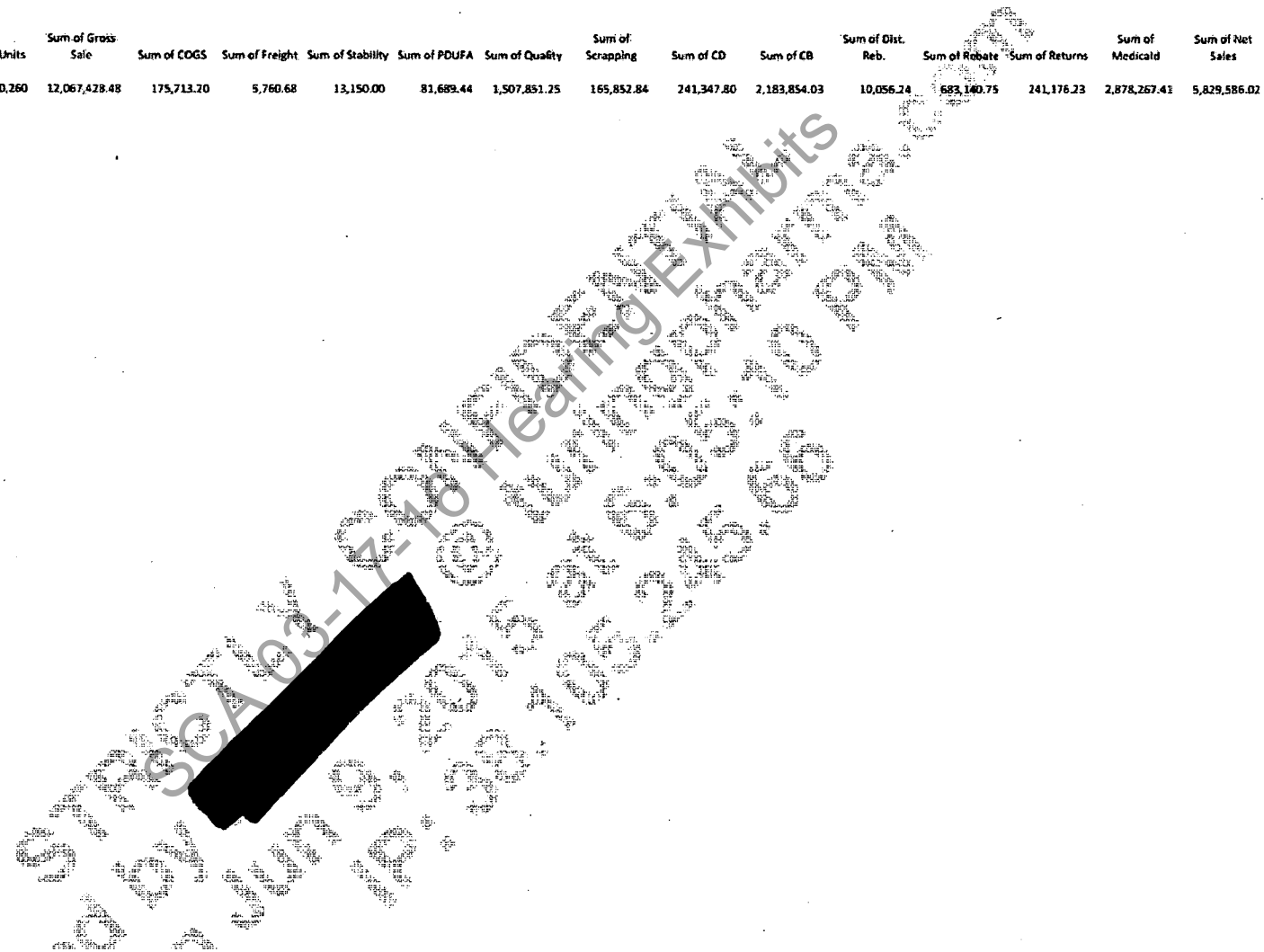
Gross to Net 2012

Row Labels	Sum of Sales quantity	Sum of Revenue	Sum of Cash Disct	Sum of Medicaid	Sum of Return	Sum of Rebates	Sum of Chargebacks	Sum of Net Sales
Daraprim 25 Mg 100 Ct	11,004.00	10,650,678.36	(213,013.72)	(1,812,186.51)	(532,533.92)	(746,746.78)	(1,725,553.28)	5,620,644.15



Gross to Net 2013

	Sum of Units	Sum of Gross Sale	Sum of COGS	Sum of Freight	Sum of Stability	Sum of PDUFA	Sum of Quality	Sum of Scrapping	Sum of CD	Sum of CB	Sum of Dist. Reb.	Sum of Rebate	Sum of Returns	Sum of Medicaid	Sum of Net Sales
Daraprim															
Daraprim 25MG 100CT	10,260	12,067,428.48	175,713.20	5,760.68	13,150.00	81,689.44	1,507,851.25	165,852.84	241,347.80	2,183,854.03	10,056.24	683,140.75	241,176.23	2,878,267.41	5,829,586.02



Gross to Net 2014

	Sum of Units	Sum of Gross Sale	Sum of COGS	Sum of Freight	Sum of Stability	Sum of PDUFA	Sum of Quality	Sum of Scrapping	Sum of CD	Sum of CB	Sum of Dist. Reb.	Sum of Rebate	Sum of Returns	Sum of Medicaid	Sum of Net Sales
Darzalex Tab 25MG 100CT	9,708	13,146,270.24	162,368.72	17,942.39	54,351.01	141,084.64	1,500,000.00	13,598.59	256,317.19	2,673,072.66	9,764.57	864,633.61	1,061,404.51	3,348,556.52	4,932,521.15

Gross to Net Q1 2015

Row Labels	Sum of Units	Sum of Gross Sale	Sum of CD	Sum of CB	Sum of Dist. Reb.	Sum of Rebate	Sum of Returns	Sum of Medicaid	Sum of Net Sales
Daraprim									
Daraprim Tab 25MG 100CT	1,836	2,488,661.28	51,003.27	398,985.85	2,290.24	183,241.72	(72,996.73)	699,471.59	1,226,665.34

	On Hand
McKesson	126
Cardinal	69
ABC	238
TOTAL	433

Material	Material Description	Batch	Vendor Ba	Expiration Date	Last Goods recei	Unit	Unrestricted Use Stock	In Quality inspection
503533	PYRIMETHAMINE, USP	A83043	13120	12/12/2015	8/9/2011	KG	0.000	2.130
503533	PYRIMETHAMINE, USP	A90905	29081	8/27/2016	2/15/2012	KG	0.000	15.170
503533	PYRIMETHAMINE, USP	AB7085	12083	8/11/2018	10/25/2013	KG	79.830	0.000

Bottles on hand: 14,887 (as of Monday, June 8)

THE PAGE (OR PAGES) OMITTED FROM THIS DOCUMENT ARE UNDER SEAL

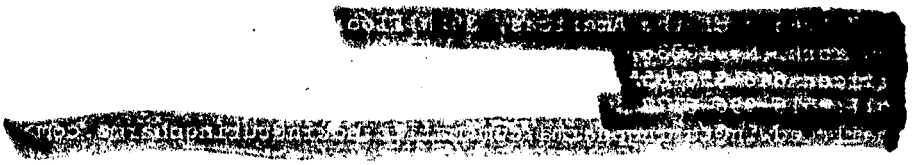
API: Pyrimethamine, USP

Fukuzyu Pharmaceutical Co., LTd.

[redacted]

From: Edwin Urrutia
To: Martin Shkreli
Sent: 6/17/2015 2:02:31 PM
Subject: Daraprim
Attachments: Daraprim.xlsx; Project Dart Model.pdf; Project Dart.pdf

Edwin Urrutia
Turing Pharmaceuticals AG
[redacted]



	Q114	Q214	Q314	Q414	Q115	Q215	Q315	Q415	2009	2010	2011	2012	2013	2014	Partial 2015	Full 2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
US HIV patients	1,100,000	1,100,000	1,100,000	1,100,000	1,111,000	1,111,000	1,111,000	1,111,000	1,046,612	1,057,078	1,067,649	1,078,326	1,089,109	1,100,000	1,111,000	1,111,000	1,122,110	1,133,331	1,144,664	1,156,111	1,167,672	1,179,349	1,191,142	1,203,054	1,215,084	1,227,235
HIV Toxo incidence	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
US HIV Tox pts	11,000	11,000	11,000	11,000	11,110	11,110	11,110	11,110	10,466	10,571	10,676	10,783	10,891	11,000	5,555	11,110	11,221	11,333	11,447	11,561	11,677	11,793	11,911	12,031	12,151	12,272
Penetration	34%	31%	31%	31%	29%	30%	30%	30%	66%	60%	60%	54%	45%	40%	30%	30%	38%	37%	4%	0%	0%	0%	0%	0%	0%	0%
US HIV Tox Daraprim Pts	933	850	853	865	803	843	843	843	6,896	6,329	6,386	5,802	4,953	4,411	1,685	3,331	4,247	4,247	425	42	4	4	4	4	4	4
Units/pt/year	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126	126
PPPY	1,708	1,708	1,708	1,708	1,708	1,708	252,000	252,000	1,172	1,172	1,172	1,449	1,782	1,708	252,000	126,854	259,560	267,347	275,367	283,628	292,137	300,901	309,928	319,226	328,803	338,667
Total HIV Tox Units	117,500	107,100	107,450	109,000	101,150	106,175	106,175	106,175	868,833	797,454	804,636	731,052	624,015	555,723	212,350	419,675	535,122	535,122	53,512	5,351	535	535	535	535	535	535
US HIV Tox Revenue	**1.6**	**1.5**	**1.5**	**1.5**	**1.4**	**1.4**	**212.4**	**212.4**	**8.1**	**7.4**	**7.5**	**8.4**	**8.8**	**7.5**	**424.7**	**427.5**	**1,102.4**	**1,135.4**	**116.9**	**12.0**	**1.2**	**1.3**	**1.3**	**1.4**	**1.4**	**1.4**
US Births	1,000,000	1,000,000	1,000,000	1,000,000	1,010,000	1,010,000	1,010,000	1,010,000	4,000,000	4,000,000	4,000,000	4,000,000	4,000,000	4,000,000	4,040,000	4,040,000	4,080,400	4,121,204	4,162,416	4,204,040	4,246,081	4,288,541	4,331,427	4,374,741	4,418,489	4,462,673
US Congenital Tox Incidence	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
US Con. Tox. pts	100	100	100	100	51	51	51	51	400	400	400	400	400	400	202	404	408	412	416	420	425	429	433	437	442	446
Penetration	24%	21%	21%	22%	40%	40%	40%	40%	34%	32%	32%	29%	25%	22%	20%	20%	20%	20%	2%	0%	0%	0%	0%	0%	0%	0%
Con. Tox. Daraprim pts	24	21	21	22	20	20	20	20	138	127	128	116	99	88	40	81	81	81	8	1	0	0	0	0	0	0
Units/pt/yr	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365	365
PPPY	4,948	4,948	4,948	4,948	4,948	4,948	730,000	730,000	3,395	3,395	3,395	4,198	5,161	4,948	730,000	367,474	751,900	774,457	797,691	821,621	846,270	871,658	897,808	924,742	952,484	981,059
Total Con. Tox. Units	8,578	7,818	7,844	7,957	7,384	7,384	7,384	7,384	50,337	46,202	46,618	42,355	36,153	32,197	14,768	29,536	29,536	29,536	2,954	295	30	30	30	30	30	30
Con. Tox. Revenue	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**14.8**	**14.8**	**0.5**	**0.4**	**0.4**	**0.5**	**0.5**	**0.4**	**29.5**	**29.7**	**60.8**	**62.7**	**6.5**	**0.7**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**
Other Infection TRx	1,152	1,050	1,053	1,068	991	99	99	99	6,758	6,202	6,258	5,686	4,853	4,322	198	1,289	397	397	40	4	0	0	0	0	0	0
Units/TRx	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
PPPY	678	678	678	678	678	678	100,000	100,000	465	465	465	575	707	678	100,000	50,339	103,000	106,090	109,273	112,551	115,927	119,405	122,987	126,677	130,477	134,392
Total Other Infection Units	57,575	52,479	52,651	53,410	49,564	4,956	4,956	4,956	337,880	310,121	312,914	284,298	242,673	216,115	9,913	64,433	19,825	19,825	1,983	198	20	20	20	20	20	20
Other Infection Revenue	**0.8**	**0.7**	**0.7**	**0.7**	**0.7**	**0.1**	**9.9**	**9.9**	**3.1**	**2.9**	**2.9**	**3.3**	**3.4**	**2.9**	**19.8**	**20.6**	**40.8**	**42.1**	**4.3**	**0.4**	**0.0**	**0.0**	**0.0**	**0.1**	**0.1**	**0.1**
Daraprim units/bottle	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Daraprim px/unit	13.55	13.55	13.55	13.55	13.55	13.55	2,000.00	2,000.00	9.30	9.30	9.30	11.50	14.14	13.55	2,000.00	1,006.78	2,060.00	2,121.80	2,185.45	2,251.02	2,318.55	2,388.10	2,459.75	2,533.54	2,609.55	2,687.83
Daraprim Px/bottle	1,355	1,355	1,355	1,355	1,355	200,000	200,000	200,000	930	930	930	1,150	1,414	1,355	200,000	100,678	206,000	212,180	218,545	225,102	231,855	238,810	245,975	253,354	260,955	268,783
Daraprim Units	205,100	206,800	224,100	221,400	200,000	118,515	118,515	118,515		1,341,600	1,157,100	1,001,777	927,400	857,400	237,031	513,643	584,483	584,483	58,448	5,845	584	584	584	584	584	584
Gross Revenue												**9.1**	**10.7**	**12.1**	**13.1**	**474.1**	**477.8**	**1,204.0**	**1,240.2**	**127.7**	**13.2**	**1.4**	**1.4**	**1.4**	**1.5**	**1.5**	**1.6**
Cash Rebate																28	28	70	72	7	1	0	0	0	0	0	0
Commercial Rebate																0	0	0	0	0	0	0	0	0	0	0	0
FFS Medicaid Rebate																48	49	122	126	13	1	0	0	0	0	0	0
Managed Medicaid Rebate																62	62	157	161	17	2	0	0	0	0	0	0
Medicare D Rebate																0	0	0	0	0	0	0	0	0	0	0	0
G2N																											
Net Revenue (mm)	**2.3**	**2.3**	**2.5**	**2.5**	**2.1**	**1.6**	**237.0**	**237.0**	**0.6**	**0.7**	**5.1**	**5.6**	**5.8**	**4.9**	**336.5**	**339.2**	**854.7**	**880.4**	**90.7**	**9.3**	**1.0**	**1.0**	**1.0**	**1.1**	**1.1**	**1.1**
Total COGS	0	0	0	0	1	1	1	1	0.0	0.7	0.6	0.5	3.6	0.4	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Gross Profit	2	2	2	2	1	1	236	236	0.6	0.0	4.5	5.1	2.2	4.5	333.5	336.2	851.7	877.4	87.7	6.3	-2.0	-2.0	-2.0	-1.9	-1.9	-1.9
R&D	0	0	0	0	0	0	1	1	0.0	0.0	0.0	0.0	0.0	0.0	4.0	4.0	4.0	4.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sales Force	0	0	0	0	0	0	30	30	0	0	0	0	0	0	30	30	30	30	0	0	0	0	0	0	0	0
FTE Salary	0	0	0	0	0.250	0.250	0.250	0.250	0.0	0.0	0.0	0.0	0.0	0.0	0.250	0.250	0.253	0.255	0.258	0.260	0.263	0.265	0.268	0.271	0.273	0.276
Sales & Marketing	0	0	0	0	0	0	2	2	0.0	0.0	0.0	0.0	0.0	0.0	3.8	3.8	7.6	7.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
G&A	0	0	0	0	0	0	0	0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OPEX	0	0	0	0	0	0	3	3	1.0	1.0	1.0	1.0	1.0	1.0	8.8	8.8	12.6	12.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Operating Income	**2**	**2**	**2**	**2**	**1**	**1**	**233**	**233**	**-0.4**	**-1.0**	**3.5**	**4.1**	**1.2**	**3.5**	**324.8**	**327.4**	**839.1**	**864.7**	**87.7**	**6.3**	**-2.0**	**-2.0**	**-2.0**	**-1.9**	**-1.9**	**-1.9**
Interest Expense									0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest Income									0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	21.3	37.9	40.3	41.2	41.9	42.7	43.4	44.2	45.0
Pre-tax Income	2	2	2	2	1	1	233	233	-0.4	-1.0	3.5	4.1	1.2	3.5	324.8	327.4	839.1	886.0	125.6	46.6	39.1	39.9	40.7	41.5	42.3	43.1
Taxes					0	0	14	14	0.0	-0.1	0.2	0.2	0.1	0.2	19.5	19.6	50.3	53.2	7.5	2.8	2.3	2.4	2.4	2.5	2.5	2.6
Net Income	**1.9**	**1.9**	**2.2**	**2.1**	**1.1**	**0.6**	**219.2**	**219.2**	**-0.4**	**-0.9**	**3.3**	**3.9**	**1.2**	**3.3**	**305.3**	**307.8**	**788.8**	**832.8**	**118.1**	**43.8**	**36.8**	**37.5**	**38.3**	**39.0**	**39.8**	**40.5**
EPS	1.94	1.92	2.15	2.15	0.54	0.29	109.58	109.58	-0.18	-0.47	1.66	1.94	0.58	1.65	152.64	153.90	394.40	416.42	59.04	21.92	18.40	18.76	19.13	19.50	19.88	20.27
S/O	1.0	1.0	1.0	1.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Cash Balance				-30	-29	-28	191	410						-30	276	276	1,064	1,897	2,015	2,059	2,096	2,134	2,172	2,211	2,251	2,291
Debt				0	0	0	0	0						0	0	0	0	0	0	0	0	0	0	0	0	0
Net Cash				-30	-29	-28	191	410	0	0	0	0	0	-30	276	276	1,064	1,897	2,015	2,059	2,096	2,134	2,172	2,211	2,251	2,291
Gross Margin	95%	95%	96%	96%	65%	53%	100%	100%						91%	99%	99%	100%	100%	97%	68%	-212%	-203%	-194%	-185%	-177%	-169%
OPEX	11%	11%	10%	10%	12%	16%	1%	1%						20%	3%	3%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
R&D	0%	0%	0%	0%	0%	0%	0%	0%						0%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
S&M	0%	0%	0%	0%	0%	0%	1%	1%						0%	1%	1%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
G&A	11%	11%	10%	10%	12%	16%	0%	0%						20%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Operating Income	84%	84%	86%	86%	53%	38%	98%	98%						71%	97%	97%	98%	98%	97%	68%	-212%	-203%	-194%	-185%	-177%	-169%
Net Income	84%	84%	86%	86%	50%	35%	92%	92%						67%	91%	91%	92%	95%	130%	469%	3825%	3786%	3748%	3710%	3672%	3635%
Revenue Y/Y			-1%	10%	0%	-14%	-25%	14655%	0%			9%	667%	10%	4%	-15%	Prorated 8997%	6777%	154%	3%	-90%	-90%	-90%	3%	3%	3%	3%
Units Y/Y			1%	8%	-1%	-10%	-41%	0%	0%			-8%	1%	-9%	-15%	-11%	-63%	-36%	147%	0%	-90%	-90%	-90%	0%	0%	0%	0%
HIV Tox TRx	1,175	1,071	1,075	1,090	1,012	1,062	1,062	1,062	6,896	6,329	6,386	5,802	4,953	4,411	3,185	4,197	4,247	4,247	425	42	4	4	4	4	4	4
Con Tox TRx	24	21	21	22	20	20	20	20	138	127	128	116	99	88	61	81	81	81	8	1	0	0	0	0	0	0
Other Infection TRX	1,152	1,050	1,053	1,068	991	99	99	99	6,758	6,202	6,258	5,686	4,853	4,322	297	1,289	397	397	40	4	0	0	0	0	0	0
Daraprim TRx	2,350	2,142	2,149	2,180	2,023	1,181	1,181	1,181	13,791	12,658	12,772	11,604	9,905	8,821	3,543	5,566	4,724	4,724	472	47	5	5	5	5	5	5
HIV Tox TRx %	50%	50%	50%	50%	50%	90%	90%	90%	50%	50%	50%	50%	50%	50%	90%	75%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
Con Tox TRx %	1%	1%	1%	1%	1%	2%	2%	2%	1%	1%	1%	1%	1%	1%	2%	1%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
Other Infection TRX %	49%	49%	49%	49%	49%	8%	8%	8%	49%	49%	49%	49%	49%	49%	8%	23%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%
Change in HIV Tox TRx						0%	0%	0%		-8%	1%	-9%	-15%	-11%	Prorated -4%	-5%	0%	0%	-90%	-90%	-90%	0%	0%	0%	0%	0%
Change in Con Tox TRx						0%	0%	0%		-8%	1%	-9%	-15%	-11%	-8%	-8%	0%	0%	-90%	-90%	-90%	0%	0%	0%	0%	0%
Change in Other Infection TRX						-90%	0%	0%		-8%	1%	-9%	-15%	-11%	-91%	-70%	0%	0%	-90%	-90%	-90%	0%	0%	0%	0%	0%
Change in Total TRx	-7%	-9%	0%	1%	-7%	-42%	0%	0%		-8%	1%	-9%	-15%	-11%	-46%	-37%	0%	0%	-90%	-90%	-90%	0%	0%	0%	0%	0%

0 Debt
0% Coupon

0 Equity
0 Share Px
0.0 New Shares
2.0 S/O

0 Total Raise
30 Purchase Px
6.0x Multiple

7% Discount
2.028 NPV

-50% Terminal Growth
2% ROIC
6% Tax

From: Karl Odquist
Sent: Tuesday, July 15, 2014 11:28 PM
To: Stephen Aselage
Cc: Bryan Selby
Subject: FW: Thiola
Attachments: Attachment

Any objection to us shipping to Kaiser? I don't imagine they are a conduit for a generic manufacturer.

KO

From: Cheryl White [redacted]
Sent: Tuesday, July 15, 2014 2:18 PM
To: June Schmidt; Karl Odquist
Subject: RE: Thiola

Hi Carl,
Per your request, please see the attachment above.

Thank you,
Cheryl

From: June Schmidt
Sent: Tuesday, July 15, 2014 4:02 PM
To: Cheryl White; Karl Odquist
Subject: Fwd: Thiola

Please forward order to Karl for approval.

Sent from my iPhone

Begin forwarded message:

> **From:** Karl Odquist [redacted]
> **Date:** July 15, 2014 at 4:29:13 PM EDT
> **To:** June Schmidt [redacted]
> **Subject: RE: Thiola**
>
> Can I preview the order? Do we know what pharmacy it is going to?
>
> KO
>
> ---
>
> **From:** June Schmidt [redacted]
> **Sent:** Tuesday, July 15, 2014 12:41 PM
> **To:** Karl Odquist
> **Subject:** Fwd: Thiola
>
> Assume this is ok to ship ?
>
> Sent from my iPhone

Begin forwarded message:

From: Cheryl White [redacted]
Date: July 15, 2014 at 8:38:41 AM EDT
To: June Schmidt [redacted]
Cc: Cheryl Gearhart [redacted]
Subject: Re: Thiola

Good Morning June,
We received an drop ship order from ABC, for 24 bottles of Thiola. Please advise.

Thank you,
Cheryl

From: Martin Shkreli
To: Michael Smith
Sent: 7/21/2015 6:03:09 PM
Subject: RE: Update

Ok go ahead

From: Michael Smith
Sent: Tuesday, July 21, 2015 6:02 PM
To: Ron Tilles; Martin Shkreli; Patrick Crutcher
Subject: RE: Update

Here is a draft of the new questions we would like to send to Impax

Project Dogwood Commercial Update

1. Please provide the distribution agreements for Daraprim, including any agreements with Walgreens Specialty Pharmacy and ICS Connect.

2. Please provide a table of all prescriptions captured by the Walgreens Specialty Pharmacy, delineating unique patient identifiers, new prescriptions, number of refills available per prescription, the quantity of pills dispensed in each prescription, dosing in each prescription and any other metrics recorded by the specialty pharmacy.

From: Ron Tilles
Sent: Tuesday, July 21, 2015 3:24 PM
To: Martin Shkreli; Patrick Crutcher; Michael Smith
Subject: FW: Update

Here you go...

From: David Ailinger [redacted]
Sent: Tuesday, July 21, 2015 2:39 PM
To: Ron Tilles
Subject: RE: Update

Ron,

We are targeting a draft to you by the end of the week. In addition, as the agreement will be subject to Board approval, we are working to schedule a Board meeting next week. We should be able to continue in parallel to expedite execution. Has Turing considered a press release and option for a joint release?

Thanks,
Dave

From: Ron Tilles [redacted]
Sent: Tuesday, July 21, 2015 2:09 PM
To: David Ailinger
Subject: Update

David,

Saw the updates thanks. Do you have time to catch up end of the day ?

Thanks,

Ron

Ron Tilles
Chairman of the Board
Turing Pharmaceuticals
[redacted]

[redacted]

From: Martin Shkreli
To: Michael Smith; Martin Shkreli
Sent: 8/5/2015 4:19:34 PM
Subject: Conversation with Michael Smith

Martin Shkreli 4:18 PM:
can u give me inventory estimates
for darprim
if worst case scenario we have to manufacture somewhere else
Michael Smith 4:19 PM:
12,521 bottles
96.460 kg of api
Martin Shkreli 4:20 PM:
so a year of bottles to go
and enough api to make how many bottles
Michael Smith 4:20 PM:
38584
prob 38,000 counting mfc slippage
Martin Shkreli 4:21 PM:
how sure are we that fukuzyu isnt making drug for someone els
Michael Smith 4:22 PM:
very unclear
i got intouch with betachem
they are trying to source cGMP API for pyrimethamine for me
Martin Shkreli 4:24 PM:
ask them if they have an exclusive with fukuzyu
and tell them we are considering acquiring the US NDA holder
Michael Smith 4:25 PM:
will do

From: Martin Shkreli
To: Stone, Adam
Sent: 8/7/2015 8:46:17 AM
Subject: Toxo Diligence

We have done a lot of diligence on toxoplasmosis, but I was very happy to speak with Dr. Rima McLeod http://www.uchospitals.edu/physicians/rima-mcleod.html who is the world expert on toxoplasmosis. One of my colleagues asked about using Bactrim instead of Daraprim. She rattled off 5 reasons why it would be unethical and unsound. She practically yelled at us for even raising it. She also endorsed our price increase if we match it with the appropriate steps to ensure access and further toxoplasmosis research. Like prior price increases we've done, she is rather lonely and no pharmas call her. This is shaping up really well.

MS

From: Martin Shkreli
To: Jim Silverman
Sent: 8/8/2015 3:43:42 PM
Subject: RE: Deal

We don't know yet but I'd say over $200m

-----Original Message-----
From: Jim Silverman [redacted]
Sent: Saturday, August 8, 2015 3:43 PM
To: Martin Shkreli [redacted]
Subject: Re: Deal

Congrats. What do you think sales will annualize at for that $55m?

Sent from my iPhone

> On Aug 8, 2015, at 11:49 AM, Martin Shkreli [redacted] wrote:
>
> Announcement Monday morning. Purchased Daraprim for $55 million.
>
> -----Original Messag[redacted]
> From: Jim Silverman [redacted]
> Sent: Saturday, August 8, 2015 11:49 AM
> To: Martin Shkreli [redacted]
> Subject: Deal
>
> Anything you can say yet?
> Saw your tweet with Patrick :)
>
> Sent from my iPhone
> NOTICE: This e-mail message (including any attachments) is a private communication and may contain confidential, privileged or proprietary information meant solely for the intended recipient. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution or copying of this communication is prohibited and may be unlawful. Please notify the sender immediately by replying to this message, then delete the e-mail and any attachments from your system.
NOTICE: This e-mail message (including any attachments) is a private communication and may contain confidential, privileged or proprietary information meant solely for the intended recipient. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution or copying of this communication is prohibited and may be unlawful. Please notify the sender immediately by replying to this message, then delete the e-mail and any attachments from your system.

From: Michael Harrison
To: Martin Shkreli; Ron Tilles; Walter C. Blum; Alan Geller; Howard Dorfman; Hirschberg, Michael
CC: Keller Perry
Sent: 7/28/2015 4:54:55 PM
Subject: BOD Meeting Thursday July 30
Attachments: #48346789v12_current_ - Turing Pharmaceuticals AG - 2015 Omnibus Incenti....docx; #48378251v10_current_ - Turing Pharmaceuticals Form of Stock Option Agre....docx; #48756944v3_current_ - Summary of 2015 Omnibus Incentive Plan.docx; #49261140v5_current_ - Turing Pharmaceuticals AG BOD- Resolutions - Equi....docx; Agenda - July 30, 2015.docx; DOCSLIB-#171088-v1-July_8,Board_Minutes.DOC; Project Dart Board Presentation.pdf

Good afternoon,

The Company would like to schedule a Board of Directors meeting this Thursday. Please see the attached agenda with exhibits. I purpose a meeting time of 1pm. Please let me know your availability.

Regards,

Michael Harrison, CPA, MST
Chief Financial Officer
Turing Pharmaceuticals
[redacted]

Turing Pharmaceuticals AG

Board of Directors Meeting

July 30, 2015

AGENDA

1. Approve July 8, 2015 board minutes (meeting minutes attached)
2. Daraprim presentation, related equity, debt and acquisition approval
3. Adopt the 2015 Omnibus Plan
4. Approve stock option awards, if applicable
5. Affirm boards knowledge and approval of the following compensatory payments:
    a. Edwin Urrutia $200,000
    b. Michael Harrison $150,000
    c. Peter Myall $100,000

Exhibits:

a) July 8, 2015 board minutes
b) Slide deck Daraprim
c) 2015 Omnibus Plan, related executive summary, sample option agreement, and related purposed resolution

MINUTES OF A MEETING OF THE BOARD OF DIRECTORS OF TURING PHARMACEUTICALS AG

July 8, 2015

A meeting of the Board of Directors (the "**Board**") of Turing Pharmaceuticals AG, a Swiss stock corporation (the "**Company**") was held via conference telephone on July 8, 2015 at 9:30am Eastern Time (US), pursuant to notice duly given.

DIRECTORS PRESENT: Ron Tilles
Martin Shkreli
Alan Geller
Walter Blum

OTHERS PRESENT: Michael Harrison
Howard L. Dorfman
Michael Hirschberg

1. Call To Order

Mr. Shkreli served as Chairman of the meeting, and Mr. Hirschberg served as Secretary and kept minutes. Mr. Shkreli called the meeting to order, announced that a quorum of the directors was present and confirmed that all participants could hear and be heard by one another. The meeting, having been duly convened, was ready to proceed with business.

2. Approval of Prior Board Meeting Minutes

Mr. Shkreli presented the directors with the minutes of the April 16, 2015 Board meeting. After discussion and upon motion duly made and seconded, it was unanimously:

> RESOLVED, that the minutes of the April 16, 2015 meeting of the Board of Directors be and hereby are approved in the form presented to the directors and affixed to these minutes.

3. Preference Shares A Offering

Mr. Shkreli advised that there was substantially increased demand from investors to participate in the Company's offering of its Preference Shares A and that the size of the offering had therefore been expanded substantially to accommodate such demand. Mr. Shkreli reported that a closing of the offering was expected within days.

4. **Approval of Statutory Auditors**

Mr. Shkreli advised that Deloitte AG had agreed to serve as the Company's Swiss statutory auditors. After discussion and upon motion duly made and seconded, it was unanimously:

> RESOLVED, that Deloitte AG be and hereby is appointed as the Company's Swiss statutory auditors subject to the approval of the shareholders at an extraordinary general meeting of the shareholders.

5. **Election of Officer**

Mr. Shkreli advised that Eliseo Salinas had been hired as the President of Research and Development of the Company. After discussion and upon motion duly made and seconded, it was unanimously:

> RESOLVED, that Eliseo Salinas be and hereby is appointed as the Company's President of Research and Development.

6. **Appointment of US Auditors**

Mr. Shkreli advised that Mayer Hoffman McCann P.C. had agreed to serve as the Company's US auditors. After discussion and upon motion duly made and seconded, it was unanimously:

> RESOLVED, that Mayer Hoffman McCann P.C. be and hereby is appointed as the Company's independent US auditors.

7. **Approval of Non-Binding Offer**

Mr. Shkreli advised that the Company had made a preliminary, non-binding $175 Million offer to acquire Symlin, a Type 1 diabetes drug, from AstraZeneca. After discussion and upon motion duly made and seconded, it was unanimously:

> RESOLVED, that the preliminary, non-binding $175 Million offer to acquire Symlin, a Type 1 diabetes drug, from AstraZeneca, be and hereby is authorized and approved.

8. **Board Expansion; Possible IPO**

Mr. Shkreli advised that the Company should consider expanding the size and scope of the Board to position the Company better for a possible initial public offering in the fourth quarter of 2015. Specifically, Mr. Shkreli suggested that the Company's goal should be to have a Board of 7 members, at least one of whom had strong pharmaceutical industry experience and one of whom had the requisite financial experience to serve as

the Chairman of the audit committee. Mr. Shkreli recommended that the Board consider adding Kenneth Banta as a director.

Mr. Shkreli then led the Board in a discussion regarding whether market volatility and international economic developments in China, Greece and Puerto Rico required the Company to move more rapidly toward an initial public offering, and the Board consensus was that, if the markets are open and the Company needs the money, it should proceed with an initial public offering sooner rather than later.

9. CEO Search

Mr. Shkreli reported that the search for a new Chief Executive Officer that had been approved at the previous Board meeting had been put on hold and that he intended to remain as the Company's Chief Executive Officer at the current time. However, Mr. Shkreli suggested that it would be appropriate to put in place a succession plan in the event that regulatory or other issues mandated that he not continue in such position. The Board enthusiastically indicated its support for Mr. Shkreli remaining as the Company's Chief Executive Officer.

There being no further business, the meeting was duly adjourned at 10:15am.

Respectfully submitted,

Michael Hirschberg
Secretary of the meeting

Approved:

_____
Martin Shkreli
Chairman of the meeting

TURING
PHARMACEUTICALS

Project Dart Board Presentation

July 2015

Executive Summary

- Turing Pharmaceuticals AG is in discussions to acquire the U.S. rights to Daraprim® (pyrimethamine) from Impax Laboratories (IPXL) for $55mm
- Daraprim® is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide, since synergism exists with this combination
  - FDA approved in January 1953 (NDA #008578)
  - Gold standard of care for toxoplasmosis
- Compelling transaction for Turing
  - 2014 U.S. net revenue of $4.9mm
  - >$500mm potential annual revenue, with >80% gross margins
  - Provides meaningful revenue diversification
  - Product already in closed specialty pharmacy distribution
  - Significantly enhances scale, expanding the platform for future growth
- Transaction to be financed with Series A proceeds and $15mm committed senior secured debt financing
  - Closed first tranche of Series A on July 23, 2015 for $62.7mm
  - Second tranche of Series A will close only if Turing consummates the acquisition
  - Fully committed debt financing from Perceptive Advisors and QVT Financial

Financing and Balance Sheet Impact

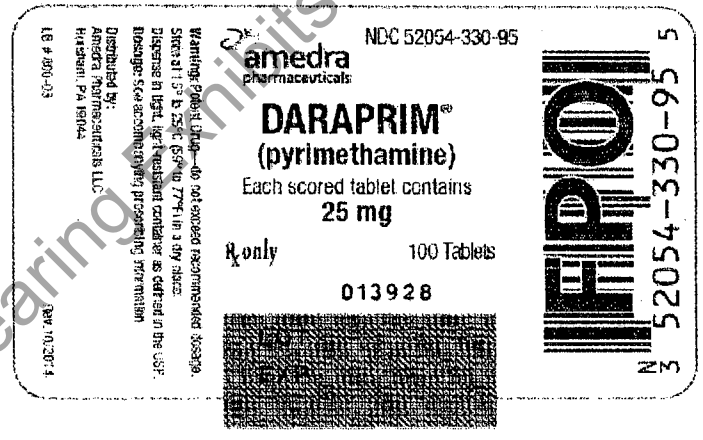
- **Transaction value of $55mm**
  - Current cash on hand of ~$37mm
  - Transaction to be financed with Series A equity raise and debt financing
- **Closed first tranche of Series A on July 23, 2015 for $62.7mm**
  - $30mm pre-money valuation
  - $39.0mm new money to the company
  - $23.7mm from conversion of existing convertible debt to Preference A shares
- **Second tranche of Series A will close only if Turing consummates the acquisition**
  - Firm indications from current shareholders to participate in second tranche for ~$15mm
- **$15mm committed senior secured debt financing for the acquisition**
  - Perceptive Advisors committed to $10mm
  - QVT Financial committed to $5mm
  - Both funds participated in Series A equity raise; Perceptive invested $8mm and QVT invested $4mm
- **Working capital of ~$10mm post the acquisition**

Debt Financing Overview

	Summary of Terms
Lenders	Perceptive Advisors and QVT Financial
Facility	Senior Secured Term Loan for $15mm
Purpose	Acquisition of U.S. rights to Daraprim
Maturity	3 years
Interest	LIBOR + 11.00%; 1.00% LIBOR floor
Amortization	Interest only for first 12 months; $250,000 monthly amortization thereafter with balance due at maturity
Origination Fee	$300,000
Warrants	35% warrant coverage; 7 year warrants with strike at Series A issue price along with customary protective provisions
Collateral	All assets of Turing Pharmaceuticals AG

Daraprim Prescribing Information and Pricing

- Daraprim® is indicated for the treatment of toxoplasmosis encephalitis
  - Approved January 23, 1953
  - No approved generics
- Current gold standard for Toxoplasmosis
  - Co-administered with sulfadiazine
  - Inhibits DHFR, disrupting folate synthesis
- Dose: 50 – 75mg/day
  - 25mg, 100 count bottle
  - ~$3,500 PPPY
- Payor Mix
  - 45% Commercial
  - 25% Medicaid
  - 25% Medicare Part D
  - 5% Cash



Actual	2011	2012	2013	2014	Q1:2015
Units (bottles)	12,600	11,004	10,260	9,708	1,836
Net Sales (mm)	$5.114	$5.620	$5.829	$4.932	$1.226

Toxoplasmosis Overview

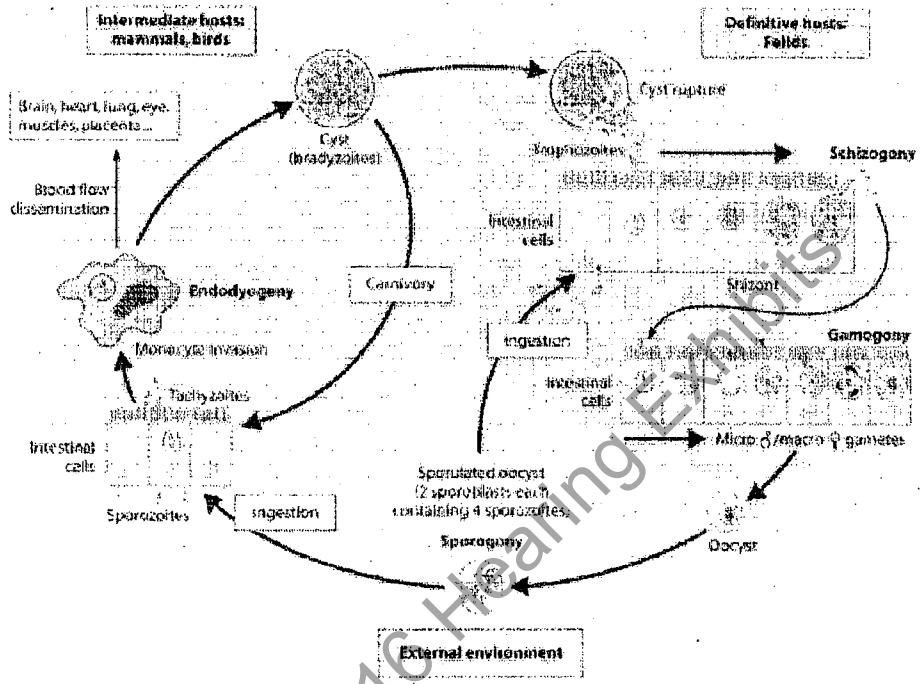


FIG 2 Life cycle of *Toxoplasma gondii*. Shown are the biology, infection, and replication of the three infective stages of the parasites in their respective hosts.

- Approximately **15%** of US population is seropositive for toxoplasmosis (30% worldwide, >50% in Brazil)
- Patients become infected by ingesting cysts in undercooked pork or oocysts in contaminated water
- Toxoplasmosis can cause severe neurological, ocular, and systemic diseases in neonates and individuals with weakened immune systems
- Symptoms self-resolve in immunocompetent hosts, though cysts containing dormant bradyzoites will remain throughout life, predominantly in the brain, CNS and musculature

Toxoplasmosis is always life threatening for neonates and the immunocompromised

Toxoplasmosis Clinical Presentation

Immunocompromised Patients

- Majority of patients are HIV positive with CD4+ counts < 100
  - Occasional incidence in immunosuppressed transplant patients
- Initially presents with non-specific symptoms such as headache, lethargy, and fever
- Disease is usually identified when patients present with difficulty walking, weakness on one side of the body (hemiparesis), seizure, speech abnormalities and loss of memory
- If untreated, further cerebral necrosis leads to dementia, status epilepticus, coma and death
- Primary lesions of cerebral necrosis, but retinal lesions are common if the infection disseminates to the eye, which can lead to blindness

Congenital Toxoplasmosis

- Estimated incidence of 1:10,000 births
- Risk of infection increases with each trimester, but infections in the first trimester lead to the most severe disease state
- Congenital infection can lead to a wide variety of manifestations including spontaneous abortion, hydrocephalus or microcephalus, CNS calcification, retinochorioditis, and failure to thrive
- Symptoms that present later in infancy and childhood include learning disabilities, growth retardation, mental retardation, convulsions, palsies, blindness and deafness

Lifecycle Management

- **Line extensions**
  - Once-a-day pill
  - Combination with sulfadiazine
  - Co-packaged combination product with folinic acid
    - Opportunity for Orphan Drug Exclusivity for the combination product
- **Next generation analogues**
  - No new medicines have been approved in more than 40 years
  - Improved potency, avoid teratogenicity
  - Target T. gondii DHFR
    - Pyrimethamine more active against human DHFR
- **Toxoplasmosis Vaccine**
  - Academics have made progress in several vaccines targeting various surface antigens
    - SAG1

Financial Projections

- **Toxoplasmosis is a rare disease and should be priced appropriately**
  - Current Hepatitis C cost for cure > $100,000
  - Net present value of HIV treatment > $250,000
  - Both significantly more prevalent and have multiple treatment options
- **Turing management has experience with niche product revenue growth strategies**
  - Specialty sales force
  - High-touch closed distribution system
  - Improved patient advocacy and support
- **Potential revenues of over $500mm with greater than 80% EBITDA margins**

Financial Model

- Illustrative Model
  - Assumes $200,000 per unit

	2011	2012	2013	2014	Partial 2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Net Revenue (mm)	**5.1**	**5.6**	**5.8**	**4.9**	**336.5**	**854.7**	**880.4**	**90.7**	**9.3**	**1.0**	**1.0**	**1.0**	**1.1**	**1.1**	**1.1**
Total COGS	0.6	0.5	3.6	0.4	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Gross Profit	4.5	5.1	2.2	4.5	333.5	851.7	877.4	87.7	6.3	-2.0	-2.0	-2.0	-1.9	-1.9	-1.9
R&D	0.0	0.0	0.0	0.0	4.0	4.0	4.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sales Force	0	0	0	0	30	30	30	0	0	0	0	0	0	0	0
FTE Salary	0.0	0.0	0.0	0.0	0.250	0.253	0.255	0.258	0.260	0.263	0.265	0.268	0.271	0.273	0.276
Sales & Marketing	0.0	0.0	0.0	0.0	3.8	7.6	7.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
G&A	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OPEX	1.0	1.0	1.0	1.0	8.8	12.6	12.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Operating Income	**3.5**	**4.1**	**1.2**	**3.5**	**324.8**	**839.1**	**864.7**	**87.7**	**6.3**	**-2.0**	**-2.0**	**-2.0**	**-1.9**	**-1.9**	**-1.9**
Interest Expense	0.0	0.0	0.0	0.0	0.0	1.8	1.2	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest Income	0.0	0.0	0.0	0.0	0.0	0.0	22.3	38.8	41.1	42.0	42.8	43.5	44.3	45.1	45.9
Pre-tax Income	3.5	4.1	1.2	3.5	324.8	837.3	885.8	125.9	47.4	40.0	40.7	41.5	42.3	43.2	44.0
Taxes	0.2	0.2	0.1	0.2	19.5	50.2	53.1	7.6	2.8	2.4	2.4	2.5	2.5	2.6	2.6
Net Income	**3.3**	**3.9**	**1.2**	**3.3**	**305.3**	**787.1**	**832.6**	**118.4**	**44.6**	**37.6**	**38.3**	**39.0**	**39.8**	**40.6**	**41.4**
EPS	1.66	1.94	0.58	1.65	43.61	112.44	118.95	16.91	6.37	5.37	5.47	5.58	5.69	5.80	5.91
S/O	2.0	2.0	2.0	2.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0
Cash Balance				12	332	1,114	1,942	2,055	2,100	2,138	2,176	2,215	2,255	2,295	2,337
Debt				0	15	10	5	0	0	0	0	0	0	0	0
Net Cash	0	0	0	12	317	1,104	1,937	2,055	2,100	2,138	2,176	2,215	2,255	2,295	2,337
Gross Margin				91%	99%	100%	100%	97%	68%	-212%	-203%	-194%	-185%	-177%	-169%
OPEX				20%	3%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
R&D				0%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
S&M				0%	1%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
G&A				20%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Operating Income				71%	97%	98%	98%	97%	68%	-212%	-203%	-194%	-185%	-177%	-169%
Net Income				67%	91%	92%	95%	131%	478%	3905%	3865%	3826%	3787%	3749%	3711%

15	Debt
12%	Coupon
75	Equity
15	Share Px
5.0	New Shares
7.0	S/O
90	Total Raise
55	Purchase Px
6.0x	Multiple
7%	Discount
2,005	**NPV**
286.45	**NPV/Share**

TURING
PHARMACEUTICALS

Project Dart Board Presentation

July 2015

From: Martin Shkreli
To: Michael Smith
CC: Nancy Retzlaff
Sent: 8/11/2015 7:56:53 PM
Subject: RE: Inventory at DCs

CAN YOU SHOW ME SOME DATA?

From: Michael Smith
Sent: Tuesday, August 11, 2015 7:53 PM
To: Martin Shkreli [redacted]
Cc: Nancy Retzlaff [redacted]
Subject: Re: Inventory at DCs

We have sales and units by pharmacy for June and July for abc and McKesson. Most stock 1-2 bottles. We can start reaching out immediately

Sent from my HTC

----- Reply message -----
From: "Martin Shkreli" [redacted]
To: "Michael Smith" [redacted]
Cc: "Nancy Retzlaff" [redacted]
Subject: Inventory at DCs
Date: Tue, Aug 11, 2015 7:47 PM

How about the pharmacies? They may still have some

From: Michael Smith
Sent: Tuesday, August 11, 2015 7:32 PM
To: Martin Shkreli [redacted]
Cc: Nancy Retzlaff [redacted]; Alyssa Palmer [redacted]
Subject: RE: Inventory at DCs

We are setting up customer accounts with each of the distributors and we are sending them credit memo for their inventory on hand at a price of old WAC ($1355.48 for everyone except walgreens, $1762.80 for walgreens).
Right now here are the current counts:

Walgreens: 64
ICS: 13
McKessen: 15
Cardinal: 0
HD Smith: 0
ANDA: 0
ABC: TBD

From: Martin Shkreli
Sent: Tuesday, August 11, 2015 7:27 PM
To: Michael Smith [redacted]
Cc: Nancy Retzlaff [redacted]
Subject: RE: Inventory at DCs

Whats the plan to buy these out?

From: Michael Smith
Sent: Tuesday, August 11, 2015 4:05 PM
To: Martin Shkreli [redacted]
Subject: FW: Inventory at DCs

At the end of July, there were 184 bottles in the big 3 wholesalers:

ABC :81
McKesson: 103
Cardinal is out

Impax also gave us contact info for the daraprim account managers at each wholesaler, so we're reaching out now

From: Alyssa Palmer
Sent: Tuesday, August 11, 2015 3:55 PM
To: Michael Smith [redacted]
Subject: FW: Inventory at DCs

Alyssa Palmer
Supply Chain Specialist | Chemistry, Manufacturing & Controls
Turing Pharmaceuticals AG
[redacted]

From: Christopher Gerber [redacted]
Sent: Tuesday, August 11, 2015 3:41 PM
To: Alyssa Palmer
Cc: Tina Ghorban; Hass Patel
Subject: RE: Inventory at DCs

Alyssa

Attached is the 852 and 867 reports for McKesson and ABC. The 852 is at the end of July and the 867 are sales for Jun and July. As I get the other information, I will forward it to you.

Thanks

Chris

[cid:image001.jpg@01D0D46F.DA7A7060]

IMPROVING HEALTH THROUGH TECHNOLOGY

Chris Gerber
Director, Pricing and Contracting

Impax Pharmaceuticals
[redacted]

From: Alyssa Palmer [redacted]
Sent: Tuesday, August 11, 2015 7:31 AM
To: Christopher Gerber
Cc: Tina Ghorban; Hass Patel
Subject: FW: Inventory at DCs

Hi Chris,

I am hoping that you will be able to support me in tracking down inventory that is currently in the distribution channels. An inventory report from early June shows a breakdown of stock between McKesson, Cardinal, and ABC. Is it possible for you to share with me the most updated sales to your partners? May also kindly ask you to share the contact information for all partners with current inventory on hand?

I am available all day today, so let me know if you prefer to discuss via phone.

Thank you,

Alyssa

Alyssa Palmer
Supply Chain Specialist | Chemistry, Manufacturing & Controls
Turing Pharmaceuticals AG
[redacted]

From: Bill Riker [redacted]
Sent: Tuesday, August 11, 2015 9:01 AM
To: Doreene Burke; Alyssa Palmer; Edward Lelina
Cc: Tina Ghorban; Hass Patel; Christopher Gerber
Subject: RE: Inventory at DCs

Hello Alyssa,

I have copied Chris Gerber on this reply. Would you please refer all question regarding his product to him?

His contact information is also listed below.

Thanks very much.

Bill

[redacted]

From: Doreene Burke
Sent: Monday, August 10, 2015 6:56 PM
To: Alyssa Palmer; Edward Lelina; Bill Riker
Cc: Tina Ghorban; Hass Patel
Subject: RE: Inventory at DCs

Hello Alyssa,

I am sharing your request with our sales team. Bill Riker could best speak to this question. Ed Lelina will support the pick-up of inventory at our UPS distribution center.

Bill,

Please review Alyssa's request about Daraprim at customers and recent sales to customers, and contact her directly with the information or any questions you might have. Thank you.

From: Alyssa Palmer [redacted]
Sent: Monday, August 10, 2015 3:37 PM
To: Edward Lelina; Doreene Burke
Cc: Tina Ghorban; Hass Patel
Subject: Inventory at DCs

Hi Ed & Doreene,

Tina has shared your contact information with me and has let me know that you might be able to support me in tracking down inventory that is currently in the distribution channels. An inventory report from early June shows a breakdown of stock between McKesson, Cardinal, and ABC. Is it possible for you to share with me the most updated sales to your partners? May also kindly ask you to share the contact information for all partners with current inventory on hand?

Thank you kindly,

Alyssa

Alyssa Palmer
Supply Chain Specialist | Chemistry, Manufacturing & Controls
Turing Pharmaceuticals AG
[redacted]

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From: Martin Shkreli
To: Greg Rea
Sent: 8/27/2015 7:24:04 PM
Subject: RE: orphan disease

I think it will be huge. We raised the price from $1,700 per bottle to $75,000. Previously impax sold 10,000 bottles per annum (50% is given away, however). So 5,000 paying bottles at the new price is $375,000,000 - almost all of it is profit and I think we will get 3 years of that or more. Should be a very handsome investment for all of us. Let's all cross our fingers that the estimates are accurate.

Martin

From: Greg Rea [redacted]
Sent: Thursday, August 27, 2015 4:21 PM
To: Martin Shkreli [redacted]
Subject: Re: orphan disease

Hi, Martin-

Yes, I received a press release about your Daraprim acquisition. What are your plans and projections for Daraprim?
Thanks.

Greg

On Thursday, August 27, 2015 3:16 PM, Martin Shkreli [redacted]

Thanks Greg! I will take a look. Did you see our acquisition? I am very excited about it.

From: Greg Rea [redacted]
Sent: Wednesday, August 26, 2015 3:37 PM
To: Martin Shkreli [redacted]
Subject: orphan disease

Hi, Martin-

Congratulations on your VTL short!
You tweeted several weeks ago about looking for other orphan disease candidates. I just saw an article posted online on 8-21-15 in "Brain" by Klein, Patzko, et.al. stating that oral inhibition of CSF1R was effective in two mice models of Charcot-Marie-Tooth Type 1. Perhaps that would be another possibility.

Best wishes,

Greg Rea

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From: Tina Ghorban
To: Michael Smith
CC: Nancy Retzlaff; Alyssa Palmer
Sent: 8/28/2015 5:09:38 PM
Subject: Re: Daraprim Buyback

Makes sense

> On Aug 28, 2015, at 3:59 PM, Michael Smith [redacted] wrote:
>
> payors won't reimburse, so I think it would increase the likelihood that a gx co gets product
>
> -----Original Message-----
> From: Tina Ghorban
> Sent: Friday, August 28, 2015 4:57 PM
> To: Michael Smith [redacted]
> Cc: Nancy Retzlaff [redacted]; Alyssa Palmer [redacted]
> Subject: Re: Daraprim Buyback
>
> If we just discontinue the NDC, we don't have to buy it back, or do we?
>
>
>
>> On Aug 28, 2015, at 3:51 PM, Michael Smith [redacted] wrote:
>>
>> Nvm, you're right. Anyway, I think we continue to have the wholesalers quarantine the product while we change the price back on the old NDC and then buy it back. It seems unlikely that they will sell it back for the old price otherwise. Also, we should tell martin ahead of doing anything.
>>
>> -----Original Message-----
>> From: Tina Ghorban
>> Sent: Friday, August 28, 2015 4:45 PM
>> To: Michael Smith [redacted]
>> Cc: Alyssa Palmer [redacted]
>> Subject: Re: Daraprim Buyback
>>
>> We changed the price on 8/11. It didn't show up in public sources because of their processes, but the effective date was the 11th.
>>
>>
>>
>>> On Aug 28, 2015, at 3:43 PM, Michael Smith [redacted] wrote:
>>>
>>> Yeah the issue is that the effective date can get backdated... we
>>> actually spoke to them before it got submitted, but then it was
>>> backdated to 8/11. I think changing the price back on the old NDC and
>>> then purchasing it back at the old price is the best way forward...
>>> so long as it's all quarantined I think it should be fine
>>>
>>> -----Original Message-----
>>> From: Alyssa Palmer
>>> Sent: Friday, August 28, 2015 4:41 PM
>>> To: Tina Ghorban [redacted]
>>> Cc: Michael Smith [redacted]
>>> Subject: RE: Daraprim Buyback
>>>
>>> Aug 13 my email correspondence starts with ABC... but we had spoken on the phone before that...
>>> Aug 11 for McKesson
>>>
>>> Alyssa Palmer

>>> Supply Chain Specialist | Chemistry, Manufacturing & Controls Turing
>>> Pharmaceuticals AG
>>> [redacted]
>>>
>>> -----Original Message-----
>>> From: Tina Ghorban
>>> Sent: Friday, August 28, 2015 4:38 PM
>>> To: Alyssa Palmer
>>> Cc: Michael Smith
>>> Subject: Re: Daraprim Buyback
>>>
>>> When did we initially reach out to them? The price was changed Tuesday the 11th.
>>>
>>> Tina
>>>
>>>
>>>> On Aug 28, 2015, at 3:32 PM, Alyssa Palmer [redacted] wrote:
>>>>
>>>> Ahhhhhhhhhhhhhhh
>>>>
>>>> -----Original Message-----
>>>> From: Tuozzo, Jennifer [redacted]
>>>> Sent: Friday, August 28, 2015 4:31 PM
>>>> To: Alyssa Palmer
>>>> Subject: RE: Daraprim Buyback
>>>>
>>>> Alyssa,
>>>>
>>>> I've received information from our data team that the price was increased a couple of weeks ago - and that the price you've noted below is incorrect. Can you please help me to understand the disconnect? What is the CURRENT WAC of this product?
>>>>
>>>> Jen
>>>>
>>>> Jennifer Tuozzo
>>>> AmerisourceBergen Corporation
>>>> Director, Global Branded Rx Sourcing Global Sourcing and
>>>> Manufacturer Relations
>>>> [redacted]
>>>>
>>>> -----Original Message-----
>>>> From: Alyssa Palmer [redacted]
>>>> Sent: Friday, August 28, 2015 3:37 PM
>>>> To: Tuozzo, Jennifer
>>>> Subject: RE: Daraprim Buyback
>>>>
>>>> Hi Jennifer, any updates? Let me know if you need any further information from me. I know you are out of the office so I just want to make sure you have everything you need.
>>>>
>>>> -Alyssa
>>>>
>>>> Alyssa Palmer
>>>> Supply Chain Specialist | Chemistry, Manufacturing & Controls Turing
>>>> Pharmaceuticals AG
>>>> [redacted]

>>>>
>>>> -----Original Message-----
>>>> From: Tuozzo, Jennifer [redacted]
>>>> Sent: Monday, August 24, 2015 4:21 PM
>>>> To: Alyssa Palmer
>>>> Cc: Michael Smith; Hamlin, Kim
>>>> Subject: Re: Daraprim Buyback
>>>>
>>>> Hello Alyssa.
>>>>
>>>> I'm working on this for you. I need to move the materials from IMPAX to Turing. Can you confirm that Turing will handle all chargebacks and returns for Daraprim? And if yes, starting on which date? Further, I will need your DUNS number and the related address. Last, can you please send over a price list with current WAC? Thank you!
>>>>
>>>> Jen
>>>>
>>>> Sent from my iPhone
>>>>
>>>>> On Aug 24, 2015, at 12:04 PM, "Alyssa Palmer" [redacted] wrote:
>>>>>
>>>>> Hi Jennifer,
>>>>>
>>>>> I am just checking in regarding any updates to the buyback of the product. I know you mentioned you were offsite this week, but I wanted to touch base to see if you needed any assistance from me or the Turing team.
>>>>>
>>>>> Thanks for everything,
>>>>>
>>>>> Alyssa
>>>>>
>>>>> Sent using OWA for iPhone NOTICE: This e-mail message (including any attachments) is a private communication and may contain confidential, privileged or proprietary information meant solely for the intended recipient. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution or copying of this communication is prohibited and may be unlawful. Please notify the sender immediately by replying to this message, then delete the e-mail and any attachments from your system.
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>>>>
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From: Redacted
Sent: Tuesday, September 23, 2014 12:38 AM
To: Martin@retrophin.com
Subject: Re: Hey

Excellent answer - thanks Martin. Appreciate the thoughtful response. I have no feel for how much momentum this may have - seems like any legislation is a long-shot for the foreseeable future in this Congress. And can't imagine this is high on the priority list. Not losing any sleep over it - but I was just curious. Generics don't do well with zero-volume drugs - just doesn't suit their model. And clearly the patient-centric approach does not fit generics well either. That said it's nice to have drugs that do have room for long-term improvement in the clinical profiles - in particular Thiola seems to have worlds of potential there.

Appreciate the thoughts - ain't us selling right now. I am very focused on the long-term (though like any fund I do get annoyed by short-term stupidity). Volume has been pretty decent. It will certainly be interesting to see the Q3 filings.

Redacted
Partner

Redacted

----- Original Message -----
From: Martin Shkreli [mailto:Martin@retrophin.com]
Sent: Monday, September 22, 2014 08:31 PM
To: Redacted
Subject: RE: Hey

It should take a long amount of time because the Sherman act clearly states companies like Retrophin and Celgene have "no duty to deal" and the Supreme Court ratified two challenges to this in the Pac Bell and Verizon cases. So if they can get some legislative momentum and get a law signed, there will still be a 'test case' which has to prove this law supersedes the Sherman Act, which you may know is one of the oldest American pieces of legislation. So I think worst case we have another 5 years because once we hand over samples to a generic, they will have to spend the next 3 years getting an ANDA approved.

Thankfully we are not selling Tracleer or Revlimid -- these drugs are so small and we do not report to IMS, so I think we will stay under the radar.

Regarding my personal investments, I cannot comment too much other than my hope is to own as much of the company as possible and I would be patient as I reengineer to put myself in a position to do so. I have a very long-term mindset. I know we have a new hedge fund shareholder who just bought 1m+ shares, so it will be interesting to know who has sold (or is selling).

MS

-----Original Message-----
From: Redacted
Sent: Monday, September 22, 2014 8:28 PM
To: Martin Shkreli
Subject: Hey

Unrelated to my previous email (but still wondering on that) - curious any thoughts on the below? Seems it could make closed distribution trickier, but I have no idea where it is going...and I have always thought true long-term barriers to entry for you guys on Chenodal/Thiola will be new formulations:
http://blogs.wsj.com/pharmalot/2014/09/19/legislation-would-prevent-drug-makers-from-thwarting-generic-riva

Redacted
Partner

Redacted

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From: Michael Harrison
To: Martin Shkreli; Ron Tilles
Sent: 10/5/2015 10:00:48 AM
Subject: Board Agenda
Attachments: Agenda - October 7, 2015.docx; July_30__2015_Board_Minutes.DOC

Martin, Ron,

Attached is the board meeting agenda and the July 30th minutes to be approved. Would you like to schedule the meeting for Wednesday, 10am?

Michael Harrison, CPA, MST
Chief Financial Officer
Turing Pharmaceuticals
[redacted]

Turing Pharmaceuticals AG

Board of Directors Meeting

October 7, 2015

AGENDA

1. Approve July 30, 2015 board minutes (meeting minutes attached)
2. Approve officer increase in salary:
   - Eliseo Salinas, President of R&D – increase in pay in the amount of 160,000 to an annual salary of $800,000
   - Michael Harrison, CFO - increase in pay in the amount of $275,000 to an annual salary of $600,000
   - Nancy Rezlaff, Chief Commercial officer - increase in pay in the amount of $250,000 to $600,000

Exhibits:

a) July 30, 2015 board minutes

MINUTES OF A MEETING OF THE BOARD OF DIRECTORS OF TURING PHARMACEUTICALS AG

July 30, 2015

A meeting of the Board of Directors (the "**Board**") of Turing Pharmaceuticals AG, a Swiss stock corporation (the "**Company**") was held via conference telephone on July 30, 2015 at 2:30pm Eastern Time (US), pursuant to notice duly given.

DIRECTORS PRESENT: Ron Tilles
Martin Shkreli
Alan Geller

DIRECTOR ABSENT: Walter Blum

OTHERS PRESENT: Michael Harrison
Howard L. Dorfman
Michael Hirschberg

1. **Call To Order**

Mr. Shkreli served as Chairman of the meeting, and Mr. Hirschberg served as Secretary and kept minutes. Mr. Shkreli called the meeting to order, announced that a quorum of the directors was present and confirmed that all participants could hear and be heard by one another. The meeting, having been duly convened, was ready to proceed with business.

2. **Approval of Prior Board Meeting Minutes**

Mr. Shkreli presented the directors with the minutes of the July 8, 2015 Board meeting. After discussion and upon motion duly made and seconded, it was unanimously:

> **RESOLVED**, that the minutes of the July 8, 2015 meeting of the Board of Directors be and hereby are approved in the form presented to the directors and affixed to these minutes.

3. **Daraprim Acquisition**

Mr. Shkreli advised the Board that the Company was considering the acquisition of the U.S. rights to DARAPRIM® (pyrimethamine) from Impax Laboratories, Inc. for a base purchase price of $55,000,000 (the "**Acquisition**"). Mr. Shkreli led the Board in a review of the Project Dart Board Presentation, a copy of which is attached hereto as Exhibit A (the "**Presentation**"), including an executive summary of the Acquisition, the financing and balance sheet impact thereof, an overview of the proposed debt financing

for the Acquisition (the "**Financing**") to be provided by Perceptive Advisors and QVT Financial, prescribing information and pricing for the product, an overview and clinical presentation of toxoplasmosis, the disease treated by the product, and financial projections for the Acquisition. Mr. Shkreli reviewed for the Board the potential risks of making the Acquisition and the potential rewards attributable thereto. After discussion and upon motion duly made and seconded, it was unanimously:

> **RESOLVED**, that the Company acquire the U.S. rights to DARAPRIM® (pyrimethamine) from Impax Laboratories, Inc. for a base purchase price of $55,000,000 plus inventory and related assets and that the Company finance a portion of such acquisition with the Financing from one or more institutional lenders, including Perceptive Advisors and QVT Financial, on substantially the terms set forth in the Presentation;
>
> **RESOLVED FURTHER**, that the authorized officers of the Company ("**Authorized Officers**") be, and each of them hereby is, authorized, directed and empowered, in the name and on behalf of the Company, to enter into such agreements and take all such actions as they, and each of them, deem advisable in order to consummate the Acquisition and the Financing.

4. **2015 Omnibus Incentive Plan**

Michael Harrison, the Chief Financial Officer of the Company, advised the Board that it would be advisable and in the best interests of the Company to establish and adopt the Turing Pharmaceuticals AG 2015 Omnibus Incentive Plan, in substantially the form provided to the Board and attached hereto as Exhibit B (the "**2015 Plan**"), subject to the receipt of shareholder approval. After discussion and upon motion duly made and seconded, it was unanimously:

> **RESOLVED**, that, effective as of the date hereof and subject to the receipt of shareholder approval, the form and terms of the 2015 Plan be, and they hereby are, approved and adopted substantially in the form attached hereto as Exhibit B;
>
> **RESOLVED FURTHER**, that, it is acknowledged and agreed that Turing Pharmaceuticals LLC, a Delaware limited liability corporation and a subsidiary of the Company ("**Turing LLC**"), shall have the authority to grant to its Eligible Employees Non-Qualified Stock Options exercisable into ordinary shares (registered shares) of the Company, each such grant to be made within the parameters of the 2015 Plan and pursuant to an award agreement signed by Turing LLC and the Company (all capitalized terms not defined herein shall have the meanings ascribed to them in the 2015 Plan);
>
> **RESOLVED FURTHER**, that the authorized officers of the Company ("**Authorized Officers**") be, and each of them hereby is, authorized, directed and empowered, in the name and on behalf of the Company, to promptly submit the 2015 Plan to the shareholders of the Company for their approval.

5. **Stock Option Grants**

Mr. Harrison advised the Board that the Company intended to present to Turing LLC its recommendations for stock option grants for the employees of Turing LLC with such options being at a strike price of $15.00 per share, for a term of ten (10) years and vesting on a quarterly basis over three (3) years commencing on September 30, 3015.

There being no further business, the meeting was duly adjourned at 3:25pm.

Respectfully submitted,

Michael Hirschberg
Secretary of the meeting

Approved:

_____
Martin Shkreli
Chairman of the meeting

EXHIBIT A

Project Dart Board Presentation

EXHIBIT B

2015 Omnibus Incentive Plan

From: Edwin Urrutia
To: Edwin Urrutia; Michael Smith; Patrick Crutcher
Sent: 10/5/2015 7:36:09 PM
Subject: Conversation with Edwin Urrutia, Michael Smith

Redacted - Not Responsive

Redacted - Not Responsive

Edwin Urrutia 1:14 PM:
http://pharmalot.com/how-martin-shkreli-prevents-generic-versions-of-his-pricey-pill/
who lets this guy speak?
Patrick Crutcher 1:16 PM:
?
Edwin Urrutia 1:16 PM:
jon haas
Patrick Crutcher 1:16 PM:
lol
Michael Smith 1:16 PM:
what is he saying
Edwin Urrutia 1:17 PM:
what isnt he saying
Patrick Crutcher 1:17 PM:
yeah i dont get why were giving out comments
Michael Smith 1:17 PM:
where did he give out a comment
Edwin Urrutia 1:18 PM:
dude are you reading?
Patrick Crutcher 1:18 PM:
oh boy , tony talking to the IT guy
Edwin Urrutia 1:18 PM:
http://pharmalot.com/how-martin-shkreli-prevents-generic-versions-of-his-pricey-pill/

o no

Patrick Crutcher 1:18 PM:

"If someone else calls and asks for 50 bottles of Daraprim, they would have to come to me for approval," explained Jon Haas, director of patient access at Turing. "Once they're set up as an approved purchasing agent, they can purchase as much as they want... It's not unique to Turing, though. It's a typical model in the industry."

Edwin Urrutia 1:18 PM:

they are neighbors

Michael Smith 1:18 PM:

just saw that

Patrick Crutcher 1:18 PM:

"Most likely I would block that purchase," he told us. "We spent a lot of money for this drug. We would like to do our best to avoid generic competition. It's inevitable. They seem to figure out a way [to make generics], no matter what. But I'm certainly not going to make it easier for them. We're spending millions and millions in research to find a better Daraprim, if you will."

Michael Smith 1:18 PM:

yeah this is ridic

Edwin Urrutia 1:19 PM:

we should not be saying shit like this
its frustrating

Patrick Crutcher 1:19 PM:

yeah

Michael Smith 1:20 PM:

yeah that is really annoying

Redacted - Not Responsive

Redacted - Not Responsive

Michael Smith 2:51 PM:
but apparently allen ripp and kevin bernier signed off on this interview
Edwin Urrutia 2:52 PM:
omg
Edwin Urrutia 2:55 PM:
thats crazy
honestly
why give interviews anymore?
Patrick Crutcher 2:55 PM:
i dont know
Edwin Urrutia 2:55 PM:
we will not change anyone's opinion
so stoopid
Michael Smith 2:56 PM:
yeah our whole co needs to stfu

Redacted - Not Responsive

Redacted - Not Responsive

Patrick Crutcher 5:09 PM:
200mm for veca / daraprim
seems light
Edwin Urrutia 5:09 PM:
yeah
Michael Smith 5:10 PM:
dara has done 28.8 gross since aug 10
Patrick Crutcher 5:13 PM:
yeah
so wed need to form whole new co around pipeline
?
Edwin Urrutia 5:36 PM:
Small, modest person, little man who works in the accounting department of a little company who drives a little car and dresses conservatively in the same clothes everyday
(clap)
Michael Smith 6:07 PM:
"I don't even say his name," Massachusetts Biotechnology Council president Bob Coughlin declared, referring to the New York drug company chief executivewho recently acquired a generic medicine to fight parasitic infections and hiked its price from $13.59 to $750.
Patrick Crutcher 6:07 PM:
lol
voldemort status
eliseo and martin still talking
Edwin Urrutia 6:08 PM:
WOW
Michael Smith 6:08 PM:
And chief executive Jeff Leiden of Vertex Pharmaceuticals in Boston, asked about Turing's 50-fold price increase at a breakfast meeting of the Greater Boston Chamber of Commerce, said simply, "We don't support that."
Patrick Crutcher 6:09 PM:
link me
Michael Smith 6:09 PM:
http://www.bostonglobe.com/business/2015/10/05/bay-state-biotech-leaders-blast-turing-ceo/i8tZ8DzwtgTirXp67UnIHL/story.html
Edwin Urrutia 6:09 PM:
read that
Edwin Urrutia 6:20 PM:
okay are we doing this?
Michael Smith 6:21 PM:
wg 27
rumor
tina

From: Tina Ghorban
To: Nancy Retzlaff
Sent: 10/10/2015 1:19:25 PM
Subject: Re: Problem:RE: need pyrimethamine

Where is this patient? Can we send them to an outpatient pharmacy?

On Oct 10, 2015, at 1:09 PM, Nancy Retzlaff [redacted] wrote:

Tina,
Can you please help Jon out here? See below. Need to respond to Rima.

N

Sent from my iPhone

Begin forwarded message:

From: Nancy Retzlaff [redacted]
Date: October 10, 2015 [redacted]
To: Jon Haas [redacted]
Subject: Fwd: Problem:RE: need pyrimethamine

Help.

Sent from my iPhone

Begin forwarded message:

From: "McLeod, Rima [OVS]" [redacted]
Date: October 10, 2015 at 12:06:14 PM EDT
To: Nancy Retzlaff [redacted]
Cc: "elise [redacted]
Subject: Re: Problem:RE: need pyrimethamine

I can see you are trying and understand that it came from something set up that you bought, but it is obligatory to fix it in real time because people suffer lifelong otherwise. It is taking too long if even one person is harmed by this. It is sounding to me so far that this patient of Paul and Lou's is the first not getting things fixed for her rapidly that I have known about.And she is in the best and most sophisticated system. I am not sure where the break down in this is. This began in August and it is far from then now. I don't want to criticize. I just want to make it right for each patient one at a time as that is where it ultimately matters. There are others very angry who will criticize but that does not solve the problem for each patient.

On 10/10/15, 8:57 AM, "Nancy Retzlaff" [redacted] wrote:

Understood. We have made progress in terms of ensuring Daraprim is widely available but we can still do better.

What we have decided to do, but it takes 4-6 weeks to become fully operational is to expand the specialty pharmacy distribution network beyond Walgreens. The previous manufacturer chose to have an exclusive arrangement with Walgreens specialty but this is clearly not appropriate for this disease. Unfortunately we're being criticized for the decisions of the previous company, but we are working to make it better.

It's your feedback and candor that has helped us quickly identify the gaps and take steps to address them.

Nancy

On Oct 10, 2015, at 11:33 AM, McLeod, Rima [OVS] [redacted] wrote:

Same day immediately not even few hours max is needed.

On 10/10/15, 8:20 AM, "Nancy Retzlaff" [redacted] wrote:

I'll follow up.

-----Original Message-----
From: McLeod, Rima [OVS] [redacted]
Sent: Saturday, October 10, 2015 11:15 AM
To: Nancy Retzlaff [redacted]
Subject: RE: Problem:RE: need pyrimethamine

Please check. There is some disconnect. Paul just now wrote: "receiving it monday" that she had not started.Then she would go to an allergist later. She should get it and go to ER with allergist if that is what is needed.Something not right or clear. Not clear why there is a difference
in what you and he write. Can you check? Not good for her if she has the
severe disease Paul described with a Guyana parasite. I am in San Diego but have asked by email the same way, and will help them. The family has
written to me but because she was complicated I left that with Paul and Louis who are good and loal, but something seems confused here. Thanks.

From: Nancy Retzlaff [redacted]
Sent: Saturday, October 10, 2015 10:07 AM
To: McLeod, Rima [OVS]
Cc: Eliseo Salinas
Subject: RE: Problem:RE: need pyrimethamine

Dear Rima,

Our list of outpatient pharmacies is growing daily. My team is checking
for accuracy and completeness. I will forward by Monday.

My understanding is that the patient received her medication yesterday. One of the members of my team spoke with Dr. Lakhani yesterday and he was
pleased with the service.

Best,
Nancy

-----Original Message-----
From: McLeod, Rima [OVS] [redacted]
Sent: Saturday, October 10, 2015 6:53 AM
To: Nancy Retzlaff [redacted]
Cc: Eliseo Salinas [redacted]
Subject: RE: Problem:RE: need pyrimethamine

Hi
Thanks! Will that list be coming soon? I think it will help.
Did the Connecticut patient receive her pyrimethamine ok?
Best wishes
Rima

From: Nancy Retzlaff [redacted]
Sent: Friday, October 09, 2015 8:31 AM
To: McLeod, Rima [OVS]
Subject: Re: Problem:RE: need pyrimethamine

We're putting together the list of outpatient pharmacies that have stock.
Stay tuned.

Sent from my iPhone

On Oct 9, 2015, at 8:55 AM, McLeod, Rima [OVS] [redacted] wrote:

Dear Nancy
This sounds like smoke and mirrors when someone's sight and life are threatened and is not acceptable. What about a small source of pre insurance free starter medications while the insurance forms are completed. Since the specialty pharmacy is open only on weekdays and specific hours it is really a problem. I mention the attorney phone call I received as a class action suit against Turing was suggested. It is for patients especially that I write, but it is also for the latter as well as an added incentive to please get this right. There really cannot be delays. People will really be hurt lifelong.You have a monopoly on safe reliable medicine right now and it truly matters for people's lives. Im sure your tired of hearing this from me and I don't want to keep writing it either, but it seems to keep re-surfacing.I know you are trying with this. Please let me know there is a workable good solution.
Thanks
Best wishes
Rima

On 10/9/15, 5:39 AM, "Nancy Retzlaff" [redacted] wrote:

Dear Rima,

I will work with Walgreens to ensure they don't miscommunicate. Walgreens is required by LAW to do an insurance verification. This is merely an administrative issue and does NOT imply that medication will be denied pending insurance. It simply means the patient needs to be triaged to the APPROPRIATE financial assistance program if required. Unfortunately the law prevents us from providing co pay assistance to government
insured patients as a for instance. There should be no issue with Medicaid patients as they pay $1 per bottle.

We have teams of people engaging with physicians and institutions to help with access to Daraprim if needed and we have stocked many hospital outpatient pharmacies.

As there are not huge numbers of patients, I'm confident that we can ensure every doctor and patient is provided with personalized service whether its from me or someone on my team.

Please continue to make us aware of any issues. It's our job and priority to ensure all patients have timely access.

Nancy

On Oct 9, 2015, at 8:23 AM, McLeod, Rima [OVS] [redacted] wrote:

Hi Nancy and Eliseo,

I am concerned for patients, and also for you as I can see that you care and are really trying to make this work, if this happens again and repeatedly.

The patient in Chicago with indemnity insurance is very smart, well educated and proactive.
By the time I had seen her she had worked with her insurance to have an over ride of the hold on the epicene And you were already working on your end to facilitate it as well.
Most patients are not like that.
She is dramatically better.

The patient of Paul*s is another proactive and well educated family I think, from the communications I have had with them.

There are many people who are not this fortunate.
They wont be as intrinsically capable and they wont find me, or you, despite all the media attention and websites etc.

Their social workers wont know of Leonora*s charity.

The only good thing about Martin*s recent social media comment that came through in the article yesterday is the comment about a vulnerable population with this disease that needs special care and attention for a nuanced and medically complicated disease.

From the news media I see that you are also preparing for a congressional investigation by today which is asking the same things I asked you re payer mix and costs and expenses.And what resources there really are left for toxoplasmosis research.Not other diseases. And how much is paying off the venture capital dept and building a different pipeline. What does it really cost a company to rovide this medicine so it helps people with all the extra distribution issues when the market is closed?

I have also gotten a call from an ambulance chasing Chicago attorney asking for persons who have been hurt by delays and lack of availability of medicine for a class action suit. It came politically motivated by virtue of the physician who referred this person to me. I told him that I knew of noone at that time.After that he did not want to talk with me more about where the problems were with access for the young woman in Indiana with restricted medicaid hmos that limit patients to access for care and make the system truly two tiered with poor care for working poor.

I am writing this particularly because I am concerned about patients and that Walgreens continue to state they are going to clear for insurance first which means that patients wait for medicines, and that is unacceptable. Can the pharmacies be informed that first doses continued until cleared is the rule? The local stocks are vital to prevent waits that harm patients and a mechanism for insurance over ride for first doses when the local stocks are not. I will watch for the list.Thanks.

Please make certain that you read this carefully and would you please let me know it has been addressed. It is really important. The other supply of pyrimethamine, which is my plan b comes from India and our pharmacy will not dispense medicines from India and China because of all the problems.Going to Canada for a three month personal supply is not fast enough or an option other than a very few locales very near the border or with lots of personal resources, so for now you are ※it" in the US as far as I can determine, and there are people who really need this medicine urgently and in real time 24/7 , as you know.There is a baby who is getting the Indian medicine in South Carolina, and Stanford is stocking that with a purity test. Our pharmacy is not doing that mentioning formaldehyde contaminating chinese products etc.

Thanks

Best wishes
Rima

On 10/9/15, 4:25 AM, "Nancy Retzlaff" [redacted] wrote:

Dear Rima,

Daraprim has been stocked at many outpatient pharmacies across the country. We can certainly provide you with that list.

I will make sure the patient has product without delay and will keep you informed.

As always, if anyone needs to speak with me please call anytime:
[redacted]

Nancy

On Oct 9, 2015, at 12:01 AM, McLeod, Rima [QVS] [redacted]>> wrote:

Dear Nancy
When will she have this?
Would you be able to forward to me the nationwide list of 100 pharmacies with phone numbers, emails and locations so it is easy to refer physicians and patients to them? Thanks.
When will this patient have her medicines. As you know from earlier it is critical that there is no wait.Treatment is urgent.
This patient is particularly problematic.
Would you let me know she has started medicine.
Paul I am at the hotel now if you wanted to phone on my cell # to discuss.
Best wishes
Rima

On 10/8/15, 7:54 PM, "Nancy Retzlaff" [redacted]>> wrote:

Dear Rima,
I called Walgreens and asked them to make it a priority.
Nancy

On Oct 8, 2015, at 8:46 PM, McLeod, Rima [QVS] [redacted]> wrote:

Hi Paul, Nancy and Eliseo,

This is not acceptable.Nancy please fix the wait re insurance check .The promise to patients was no wait for first doses.This is harmful to wait. Same as the girl in Indiana, in Chicago etc. Must be there when physician sees patient first doses.

Paul if you can aspirate aqueous for organism and drug sensitivity testing (we can do this if Louis can sub inoculate) . Her husband mentioned Dr. Weiss so I am assuming he is involved too. I think I suggested both you and Louis when I spoke
with them.

Need to have it same day without any stipulation re insurance check.
Especially this patient who is very complicated with a likely hyper virulent organism, severe disease, prior exposure to meds, and lots of hypersensitivity. This may the first person harmed by delays if there are any. I am on an airplane flying to San Diego. She must have first doses asap. Which is the University Hospital with the meds in stock in Manhattan or where she is in Connecticut. Paul standard adult doses for atovaquone, think

about malarone as atovaquone alone is a problem.
You
might also think about itraconazole from Gettysburg meeting as second agent but no experience in people at all. From her husband sounds like she has very significant allergy. And from her history sounds like she has something bad from Guyana. You might want to reach out to Daniel AZjenberg, Marie Laure Darde and Carme to ask what sensitivity testing and responsiveness they have. And whether they see atopy like she has in terms of T cell dysregulation by parasite.

I will have my cell on when I land in 2.5 hours. Cell [redacted]
Fatima also reached out to her husband. I am concerned about this patient. Nancy and Eliseo please make certain she has medicines quickly today no wait. Cant wait for insurance clearance as you said would always be the case.

Thanks
Best wishes
Rima

From: pl [redacted]
Sent: Thursday, October 08, 2015 3:45 PM
To: Nancy Retzlaff
Cc: Eliseo Salinas; McLeod, Rima [OVS]
Subject: Re: need pyrimethamine

Hi Nancy,

Thanks for the follow-up. I separately called Walgreen's and put her in the system.

I'll keep you posted if there is a problem. They said she may be able to get it as early as tomorrow but they have to coordinate with her insurance.

My office number is [redacted]. Today is a good day to talk. Tomorrow please coordinate with Corinne, my clinical assistant, if the call needs to wait until tomorrow.

Thanks,
Paul Latkany, M.D.

From: Nancy Retzlaff [redacted]
To: pl [redacted]
Cc: Eliseo Salinas [redacted]
Sent: Thursday, October 8, 2015 3:45 PM
Subject: Re: need pyrimethamine

At what number can we reach you?

On Oct 8, 2015, at 3:37 PM, pl [redacted] wrote:

Hi Nancy,

What do I do to have the patient get the medicine? Please advise?

I would like her to get 50mg per day of pyrimethamine.

Thanks,

Paul Latkany, MD.

From: Nancy Retzlaff [redacted]
To:
Cc: pl [redacted]; Eliseo Salinas [redacted]
Sent: Sunday, October 4, 2015 9:21 AM
Subject: Re: saw new pt from ct

Dear Dr. Latkany,

Per Dr. McLeod I'm reaching out to offer assistance regarding access to Daraprim. Should you encounter any issue, please reach out so we can help. First step is to go to Daraprimdirect.com<http://daraprimdirect.com><http://daraprimdirect.com/>.

Best,
Nancy

On Oct 3, 2015, at 11:04 PM, McLeod, Rima [OVS] [redacted] wrote:

Hi
Are the hives with azithromycin for certain?
Atovaquone is not a very good second drug. But you don易t really have much option.
Another possibility might be malarone(atovaquone proguanil) plus pyrimethamine plus folinic acid.
Probably would start as you write with pyrimethamine atovaquone , leucovorin,How much does she weigh.
Dr.Latkany is in Manhattan.
The uveitis is not related to intraocular clinda?

Thanks.
Paul, please let me know how she does.

Are you able to obtain pyrimethamine?
Does your pharmacy have some now for first doses.
There is a new system where you need to complete a form.It can be obtained

easily.www.daraprimdirect.com/<http://easily.www.daraprimdirect.com/><http://easily.www.daraprimdirect.com/ Nancy can you please reach out to Dr.Latkany to see if he needs help or his patient needs any help with either acces with no wait, or later insurance.

Sounds serious and complicated in terms of medicines as no second line meds that are very good available.

Paul, warm wishes to you,Monica and the kids.If you want to phone to discuss further [redacted].
Rima

From: pl

[redacted]
Reply-To: pl

[redacted]
Date: Saturday, October 3, 2015 at 9:36 PM
To: Rima McLeod

[redacted]
Subject: saw new pt from ct

HI Rima,

I saw a new patient from ct today. Very complex history that still needs to be sorted out. However, I'm treating her as if she has toxoplasma. She has allergy with hives to bactrim clindamycin and azithromycin.

I'm thinking atovaquone and pyrimethamine with prednisone.

There is no view she has 3 plus anterior cell left eye. no view posterior with a history of several injections of clindamycin intravitreal despite history of hives to clindamycin?

She was also labeled as having kikuchi disease. The unifying diagnosis is toxoplasmosis but to be clear I have no view of the lesion.

Thanks,
Paul

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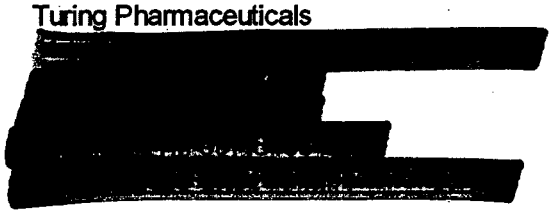
From:	Michael Harrison
To:	Martin Shkreli; Ron Tilles; Walter C. Blum; Alan Geller; Hirschberg, Michael
Sent:	10/12/2015 11:43:11 AM
Subject:	10/14 Meeting Agenda and Exhibits
Attachments:	2015.09.29 Schmidt ltr to Turing c.o Weiner.pdf; Agenda - October 14, 2015.docx; July 30, 2015 Board Minutes.doc; Registered letter_9_6_2015_EN.DOCX; September 24, 2015 Board Minutes.doc

Please find attached the 10/14 meeting agenda and exhibits.

Michael Harrison, CPA, MST
Chief Financial Officer
Turing Pharmaceuticals



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Turing Pharmaceuticals AG

Board of Directors Meeting

October 6, 2015

AGENDA

1. Approve July 24th and July 30th board minutes (meeting minutes attached)
2. Approve officer increase in salary:
   - Eliseo Salinas, President of R&D – increase in pay in the amount of 160,000 to an annual salary of $800,000
   - Michael Harrison, CFO - increase in pay in the amount of $275,000 to an annual salary of $600,000
   - Nancy Rezlaff, Chief Commercial officer - increase in pay in the amount of $250,000 to $600,000

3. Next steps regarding investigations from district attorney of the Canton of Zug and the U.S. Federal Trade Commission

Exhibits:

a) July 24 board minutes
b) July 30 board minutes
c) Registered Letter from district attorney of Canton of Zug
d) Non-public Letter from the FTC

MINUTES OF A MEETING OF THE BOARD OF DIRECTORS OF TURING PHARMACEUTICALS AG

July 30, 2015

A meeting of the Board of Directors (the "**Board**") of Turing Pharmaceuticals AG, a Swiss stock corporation (the "**Company**") was held via conference telephone on July 30, 2015 at 2:30pm Eastern Time (US), pursuant to notice duly given.

DIRECTORS PRESENT: Ron Tilles
Martin Shkreli
Alan Geller
Walter Blum

OTHERS PRESENT: Michael Harrison
Howard L. Dorfman
Michael Hirschberg

1. Call To Order

Mr. Shkreli served as Chairman of the meeting, and Mr. Hirschberg served as Secretary and kept minutes. Mr. Shkreli called the meeting to order, announced that a quorum of the directors was present and confirmed that all participants could hear and be heard by one another. The meeting, having been duly convened, was ready to proceed with business.

2. Approval of Prior Board Meeting Minutes

Mr. Shkreli presented the directors with the minutes of the July 8, 2015 Board meeting. After discussion and upon motion duly made and seconded, it was unanimously:

> **RESOLVED**, that the minutes of the July 8, 2015 meeting of the Board of Directors be and hereby are approved in the form presented to the directors and affixed to these minutes.

3. Daraprim Acquisition

Mr. Shkreli advised the Board that the Company was considering the acquisition of the U.S. rights to DARAPRIM® (pyrimethamine) from Impax Laboratories, Inc. for a base purchase price of $55,000,000 (the "**Acquisition**"). Mr. Shkreli led the Board in a review of the Project Dart Board Presentation, a copy of which is attached hereto as Exhibit A (the "**Presentation**"), including an executive summary of the Acquisition, the financing and balance sheet impact thereof, an overview of the proposed debt financing for the Acquisition (the "**Financing**") to be provided by Perceptive Advisors and QVT

Financial, prescribing information and pricing for the product, an overview and clinical presentation of toxoplasmosis, the disease treated by the product, and financial projections for the Acquisition. Mr. Shkreli reviewed for the Board the potential risks of making the Acquisition and the potential rewards attributable thereto. After discussion and upon motion duly made and seconded, it was unanimously:

RESOLVED, that the Company acquire the U.S. rights to DARAPRIM® (pyrimethamine) from Impax Laboratories, Inc. for a base purchase price of $55,000,000 plus inventory and related assets and that the Company finance a portion of such acquisition with the Financing from one or more institutional lenders, including Perceptive Advisors and QVT Financial, on substantially the terms set forth in the Presentation;

RESOLVED FURTHER, that the authorized officers of the Company ("**Authorized Officers**") be, and each of them hereby is, authorized, directed and empowered, in the name and on behalf of the Company, to enter into such agreements and take all such actions as they, and each of them, deem advisable in order to consummate the Acquisition and the Financing.

4. **2015 Omnibus Incentive Plan**

Michael Harrison, the Chief Financial Officer of the Company, advised the Board that it would be advisable and in the best interests of the Company to establish and adopt the Turing Pharmaceuticals AG 2015 Omnibus Incentive Plan, in substantially the form provided to the Board and attached hereto as Exhibit B (the "**2015 Plan**"), subject to the receipt of shareholder approval. After discussion and upon motion duly made and seconded, it was unanimously:

RESOLVED, that, effective as of the date hereof and subject to the receipt of shareholder approval, the form and terms of the 2015 Plan be, and they hereby are, approved and adopted substantially in the form attached hereto as Exhibit B;

RESOLVED FURTHER, that, it is acknowledged and agreed that Turing Pharmaceuticals LLC, a Delaware limited liability corporation and a subsidiary of the Company ("**Turing LLC**"), shall have the authority to grant to its Eligible Employees Non-Qualified Stock Options exercisable into ordinary shares (registered shares) of the Company, each such grant to be made within the parameters of the 2015 Plan and pursuant to an award agreement signed by Turing LLC and the Company (all capitalized terms not defined herein shall have the meanings ascribed to them in the 2015 Plan);

RESOLVED FURTHER, that the authorized officers of the Company ("**Authorized Officers**") be, and each of them hereby is, authorized, directed and empowered, in the name and on behalf of the Company, to promptly submit the 2015 Plan to the shareholders of the Company for their approval.

5. **Stock Option Grants**

Mr. Harrison advised the Board that the Company intended to present to Turing LLC its recommendations for stock option grants for the employees of Turing LLC with such options being at a strike price of $15.00 per share, for a term of ten (10) years and vesting on a quarterly basis over three (3) years commencing on September 30, 3015.

There being no further business, the meeting was duly adjourned at 3:25pm.

Respectfully submitted,

Michael Hirschberg
Secretary of the meeting

Approved:

_____
Martin Shkreli
Chairman of the meeting

EXHIBIT A

Project Dart Board Presentation

EXHIBIT B

2015 Omnibus Incentive Plan

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MINUTES OF A MEETING OF THE BOARD OF DIRECTORS OF TURING PHARMACEUTICALS AG

September 24, 2015

A meeting of the Board of Directors (the "**Board**") of Turing Pharmaceuticals AG, a Swiss stock corporation (the "**Company**") was held via conference telephone on September 24, 2015 at 12:00pm Eastern Time (US), pursuant to notice duly given.

DIRECTORS PRESENT: Ron Tilles
Martin Shkreli
Alan Geller
Walter Blum

OTHERS PRESENT: Michael Harrison
Michael Hirschberg

Mr. Shkreli served as Chairman of the meeting, and Mr. Hirschberg served as Secretary and kept the minutes. Mr. Shkreli called the meeting to order, announced that a quorum of the directors was present and confirmed that all participants could hear and be heard by one another. The meeting, having been duly convened, was ready to proceed with business.

Mr. Shkreli reported on the media uproar which he and the Company had been experiencing for the past week related to the Daraprim acquisition and increase in product price. Mr. Shkreli indicated that, while he personally was being painted as the villain, the publicity had actually validated the value and importance of the drug itself and that sales projections remained strong. He posited to the Board that the easiest response to the media and political situation, and the one that would avoid problems with auditors, the SEC and other pharmaceutical companies who might sell additional assets to the Company, would be for him to resign as Chief Executive Officer and member of the Board and have the Company bring in a new seasoned senior executive with deep pharmaceutical experience to lead the Company. In connection therewith, Mr. Shkreli requested that the other directors meet Daniel Tasse, who might be a possible replacement for Mr. Shkreli as Chief Executive Officer and a director of the Company.

Mr. Shkreli advised the Board, however, that he was not inclined at the present time to make any change in his role in the Company but asked for opinions from the other directors on the issue of his remaining as the Company's Chief Executive Officer. A discussion ensued about the state of mind of the Company's employees, the economics of the Daraprim purchase, the impact of the negative publicity on the Company's business strategy going forward and what is best for the Company.

Mr. Shkreli reported that, in his view, there should be no change in the Company's overall business model, the pipeline of prospective product purchases had not been adversely affected, the mood of the Company's employees appeared fine and none of the Company's employees wanted him to resign as Chief Executive Officer. Mr. Shkreli suggested that the Board continue to think about and discuss the issues.

There being no further business, the meeting was duly adjourned at 12:30pm.

Respectfully submitted,

Michael Hirschberg
Secretary of the meeting

Approved:

_____
Martin Shkreli
Chairman of the meeting

UNITED STATES SENATE

SPECIAL COMMITTEE ON AGING

Interview of Martin Shkreli

by Matthew Herper

Forbes Healthcare Summit

December 3, 2015

[TRANSCRIPT PREPARED FROM A VIDEO RECORDING.]

PROCEEDINGS

SPEAKER: Ladies and gentlemen, now please welcome to the stage interviewer Matthew Herper and Martin Shkreli, founder and CEO, Turing Pharmaceuticals.

MR. HERPER: All right, Martin. Well, thanks for coming.

MR. SHKRELI: Thank you.

MR. HERPER: So, a few months ago on national TV, you said that you at least would think about lowering the price of Daraprim from the level to which you'd raised it after buying it. You decided not to do that. Why?

MR. SHKRELI: Well, so, I think there's two reasons, uh, probably the reason we said and then the reason we didn't say too much about it, and I'll go through both.

The first reason is, well, we talked to our customers and they--the biggest complaint we had was hospital customers getting Daraprim. So, we're lowering the price for them. To be fairer to me, we did lower the price for the hospital customers, and we are releasing a smaller bottle, which is, I think, almost ready to hit the shelves now, which will make it much more easy--much easier for hospitals to afford. So, that's sort of the primary reason. We talked to our customers and we--you know, that's what they wanted.

The second reason we didn't talk about much, but I'll

tell you here today--

MR. HERPER: Mm-hmm.

MR. SHKRELI: --is that we have shareholders. We have shareholders just like every other company and our shareholders want us to maximize our profits, and lowering the price of our product is in direct contrast to achieving that objective. Under Delaware law, companies are by law required to maximize opportunities for shareholders, especially--especially to maximize them when there's a conflict of doing something good for yourself versus doing something good for your shareholders. By law, you absolutely have to do what's good for your shareholders.

And it would be better for me to not lower the price--to not--to lower the price. I wouldn't be in the hot seat with you. But, the reality is, my duty is to my shareholders, and if I don't maximize opportunity for my shareholders and do something for my own vanity, which I think a lot of people do, I could get sued for that, and it's wrong. It's not--

MR. HERPER: You're worried about getting sued? Martin Shkreli is worried about getting sued?

MR. SHKRELI: No, definitely not worried about getting sued, but I'm worried about doing something for my own benefit, like not being so much in the crosshairs of folks at the--at the expense of my shareholders, who is my--that's

my primary duty. It's called fiduciary duty. It's not a new concept.

MR. HERPER: No, it's not a new concept. Why--so, why is Daraprim sold under a closed restricted system? I mean, this is fairly key to your ability to maintain this price. What's the justification here? Initially, this was used for drugs that are unsafe or have side effects. What--why is it okay to do here?

MR. SHKRELI: I think almost every very expensive drug is sold under closed distribution because it's--it's such a complicated reimbursement process that it's better for the patient to not go to the pharmacy and get--the pharmacist--

MR. HERPER: So, it's in--your closed distribution system is for the--is to counter the financial toxicity that you've created?

MR. SHKRELI: [Laughs.] No. It's to help patients with--every company does it, that any company that has a drug that's a very expensive product, by far and away, the best way to do it is through a closed system. I mean, that's well known.

MR. HERPER: But--so why should this be an expensive drug?

MR. SHKRELI: Umm, I'd say--I'd--I'd--so--so, there's a number of reasons, but probably the first reason I'd go through is the one I--I walked through earlier that we don't

talk about a lot, which is our shareholders expect me to make as much money as possible for them, and that's the ugly, dirty truth. And I raised $100 million in our Series A, which is the fourth-largest Series A ever for drugs in two weeks, without a road show. I picked up the phone, made a few phone calls. I got $100 million in the bank.

And, my investors know what I do with that money. I multiply it for them. That's my job. Umm, and I do it really well and I'm going to keep doing it, and that's part of what capitalist America is all about, and as long as patients don't suffer, which we've bent over backwards to make sure they don't, and we're responsible with the profits, we're not taking those profits and endowing a library in my name or something, we're taking the profits and doing research with the money.

MR. HERPER: But drug prices are supposed to be--it's supposed to be an incentive system.

MR. SHKRELI: I don't know what it's supposed to be. It's a business. We're supposed to make as much money as possible, Matt. I mean, at the end of the day, I just explained that there is a fiduciary duty to shareholders and I cannot break that duty because you tell me to or because some magazine is going to say, what a bad guy. It doesn't work that way.

MR. HERPER: And, is there--is there a duty to society?

Is there a duty to patients?

MR. SHKRELI: I know that society can't put you in jail for violating fiduciary duty, but the federal government can. So, I think that, you know, I take the law very seriously. Delaware law is explicit. You must maximize shareholder opportunities.

And, by the way, if I wasn't known to do that, I'd have a lot harder time raising money. I mean, I'm--I'm shortly going to announce a deal where I'm buying a company that is out of money--

MR. HERPER: So, you're announcing--you're announcing that you're going to announce a deal?

MR. SHKRELI: Yes.

[Audience laughter.]

MR. SHKRELI: That is what I'm doing. Umm, and--and so the point is--you know, you know our business model. We look at, you know, 30, 40, 50 deals at a time, and, you know, a good half of those companies that we're acquiring are developing really interesting, cool drugs that need incentive--need that incentive system you're talking about, need financing. But, a good half of them are out of business, and I don't like being out of business. I don't like when my employees need to be fired. I don't like when my stockholders are angry at me. So, I'm going to maximize profits, and, you know, whatever you say about, you know,

how the system works and so forth, at the end of the day, I think that's what people are afraid to say.

It's probably what Horizon, one of your sponsors, in fact, is afraid to say after doing lots of price increases themselves, and Valiant and others. Not to pick on Horizon. It's a great company. It just happens to be right in my face. The--you know, the idea that, you know, there's something wrong with capitalism and that pharmaceuticals are exempt from capitalistic ideals, it's insane.

MR. HERPER: So, you say that--that patients still have the access they had before.

MR. SHKRELI: Yeah.

MR. HERPER: Are you sure?

MR. SHKRELI: Mm-hmm.

MR. HERPER: Because it does look like Express Scripts--so, I will consider the source--but Express Scripts does say that their--that their volumes of Daraprim went down after the price increase within the system. And there have been--there have been case reports of, for instance, an HIV reporter at Tucson--this was in November, and this was--this is through the IDSA--but, after a lapse in the patient's care, his C4 count went up. At the time of his return to care, he did not have health insurance. I ordered Daraprim for him and our pharmacy could not get it for him for multiple reasons. It--cost prohibitive even with 340(b)

pricing and it also required paperwork which would delay access. And after multiple phone calls, the patient was switched to atovaquone. So, there's a--and there are stories like this. There are people who don't--

MR. SHKRELI: Yeah--

MR. HERPER: --the drug because--

MR. SHKRELI: I don't think so. So--so, there's a number of conflu--confounding factors that are pretty important to understand here. The--when we buy--bought this drug, our--the prior owner was in the midst of changing the distribution system. They did that without our prompting, by the way. We were going to do that, make no mistake about it. We were going to do it ourselves. But, uh, we were shocked.

We were actually in discussions with Express Scripts--I can reveal this--and Express Scripts e-mailed me the other day begging for our business. Uh, I can send you that e-mail if you'd like. Umm, they wanted to distribute Daraprim, and instead--and we actually gave--we said, when we buy this drug, we'll give you the contract, and they were thrilled. And then what we saw, amazingly, Express Scripts sent us an e-mail and they said, well, it turns out that we got this e-mail from Impax that says that Walgreens is going to be the distributor of record. And, we said, well, it looks like you're--you're SOL. Most of you know what that

is, I think. And, they're out of luck.

And, uh, the--so, we told Express Scripts, we're sorry, we can't distribute Daraprim, which is--you know, they're going to lose out on five, ten million dollars of fees. So, I don't know if this reaction is something, you know, is related to that. But, the point of my story is that the distribution change, which was not authorized or expected, quite frankly, by us, that disintermediated and--and caused all these eruptions.

I want to go post hoc ergo propter hoc with our company. We've done everything possible to make sure everyone can get the drug. This is the prior manufacturer's fault.

MR. HERPER: Even if it's recent.

MR. SHKRELI: It's not--it's--they changed the distribution just before we bought the drug and they didn't tell anyone. They didn't put out a sales force. We hired 50 people to go get the word out on how to--how to get our product. I personally answer product acquisition phone calls. I dealt with the--with Mass General on getting, uh, illegal aliens' pill for free. Sixty-five percent of our drug, we sell for a penny. Uh, so I--I don't really think it makes a lot of sense. We've got 200 people at Turing that are dedicated to make sure everyone gets their medicine. And, by the way, that's 200 more people than

anyone ever--has ever had for this medicine.

MR. HERPER: But, do patients need 200 people dedicated to getting them their medicine at the previous price? I mean, this drug is produced as a generic at much lower prices--

MR. SHKRELI: Yeah.

MR. HERPER: --elsewhere in the world, and is being compounded at a much cheaper price than you're charging, which has got to be a lot more expensive than manufacturing it.

MR. SHKRELI: Yeah. No, I'll just go back to my prior statement. I mean, we--like most companies, we have a duty to maximize our profits. You know, Coca-Cola has a duty to do it. Proctor and Gamble and has a duty to do it. And so do we.

MR. HERPER: You think there's absolutely nothing wrong with what you're doing?

MR. SHKRELI: Absolutely not.

MR. HERPER: Does anyone want to ask a question? Oh, well--

MR. SHKRELI: Bring it on.

MR. GERMAIN: Hey, thanks. Will Germain, New York One-

-

MR. SHKRELI: Are you the cameraman?

MR. GERMAIN: Yeah--

MR. SHKRELI: Jesus Christ.

MR. GERMAIN: Well, I'm a reporter, camera guy--

MR. SHKRELI: Okay.

MR. GERMAIN: --do it all these days. Umm, okay. So, two quick questions. One--

MR. SHKRELI: One. Sorry.

MR. GERMAIN: The explanation for your pricing strategy seems to be based mostly on an economic justification--

MR. SHKRELI: Well, you know, I mean, the one I'm giving out that I haven't given out before. There's a-- there's an R&D justification, too.

MR. GERMAIN: So, I mean, do the ethics come into play at all in your mind when creating pricing strategies like this?

And then my second question is--

MR. SHKRELI: No second question, sorry.

MR. GERMAIN: --umm, if what you're doing--

MR. SHKRELI: Matt was explicit that there would be one question.

MR. GERMAIN: Well, this--this ties in. If what you're doing really is legal and right as far as the eyes of the law are concerned, then can you explain why you're the subject of multiple federal investigations right now, one from the United States Attorney's Office for the Eastern District of New York and from a United States Senate

committee?

MR. SHKRELI: Yeah. Well, I'll take your second question first, because it's--it's more interesting. I mean, politicians love to beat up on guys that are seen to be, you know, public kind of--public enemies, if you will. You know, that's--that's a great way to get elected. That's a great way to get your--

MR. GERMAIN: It's an even better way to get elected if you put them in jail.

MR. SHKRELI: It is. Uh, just ask--just ask our friend Eliot Spitzer. But, the--at the end of the day, the--you know, that sort of--that comes with the territory.

With respect to your first question, which was--

MR. GERMAIN: It was ethics.

MR. SHKRELI: Yeah. So, you know, I--I read a lot of my business trading from Warren Buffett, and in the '60s and '70s, Warren Buffett bought a company called See's Candy, and Buffet bragged in his letters about raising the price of See's Candy every year. Every year, he got away with big, big price increases. And as a capitalist, it's your favorite thing, is pricing power. And at the end of the day, if you want all corporations to not have the obligation to maximize shareholder duty, we should take a big old vote and have the Senate and Congress change the law. But right now, that's the law and our job is to--as executives of a

company is to maximize shareholder duty. It's--you know, last time I read carefully, you know, the laws, ethics are--one's general conception of ethics are generally not at play here.

MR. HERPER: Another one? Up here.

MS. WHITE: Hi, I'm Kym White with Edelman, and I have two questions for you. The first is, if you could rewind the clock a few months, I wonder if you would do anything differently.

And the second is, I'd like to know if you think corporate reputation matters.

MR. SHKRELI: I probably would have raised the price higher, is probably what I would have done. Umm--

MR. HERPER: Why?

MR. SHKRELI: I--I think health care prices are inelastic. I could have raised it higher and made more profits for our shareholders, umm, which is my primary duty. And, again, no one wants to say it, no one's proud of it, but, uh, this is a capitalist society, capitalist system, and capitalist rules, and my investors expect me to maximize profits, not to minimize them, or go half, or go 70 percent, but to go to 100 percent of the profit curve that we're all taught in MBA class.

The second question is about reputation--

MR. HERPER: But, if you're maximizing profit for your

shareholders, why aren't--why are you spending it on R&D?

MR. SHKRELI: Well, that's going to maximize long-term earnings.

MR. HERPER: Okay.

MR. SHKRELI: So, those R&D investments, we hope to make ten, 20, 50 times our money on.

MR. HERPER: And, so, essentially here, you think that patients aren't being harmed and that, umm, and that you're actually doing more R&D, which is good for the long term.

MR. SHKRELI: Yeah. And I think if you question all of this--

MR. HERPER: I mean, are you Robin Hood, stealing from the insurers and giving to the R&D community, is that the--

MR. SHKRELI: Maybe, but before--before we self-label ourselves, I think the--the harder thing is, you know, try to be a CEO yourself. See how it goes. Try to maximize profits and not get kicked out of a company and, uh, and let me know how that goes for you. You know, price drugs really low. You won't last very long. You know, it's people that--that are willing to make these hard choices, grow earnings for their shareholders, and, again, try to do the right thing with those profits, umm, and make sure that no patient is left behind, make sure that we invest in a disease that hasn't had a new investment in 70 years. We're sitting on one drug for toxoplasmosis that's 70 years old. You don't

have to have a Ph.D. in infectious diseases to know that's a dangerous, dangerous place to be. We are developing three new drugs for toxoplasmosis, which, by the way, will be very expensive if they ever get approved, but hopefully will replace pyrimethamine as the backbone of therapy that we've been relying on too long. It'd be like interferon still being the backbone for Hep C. It wasn't a pretty picture and we're all happy that Gilead is here, right?

MR. HERPER: So, does corporate reputation matter to you?

MR. SHKRELI: I think it does. Umm, you know, I think that, you know, we just announced a deal with the Sick Kids' Hospital and Toronto University. We're proud to announce that. It was yesterday or today. And, we're developing the first-ever drug for a rare disease called--

MR. HERPER: But, you're--I mean, you're sacrificing a huge amount of corporate--

MR. SHKRELI: I don't think so. I'm explaining to you right now that--that we signed a major agreement with a major research university to develop a rare disease drug for Lafora disease. They could have gone to Isis. They could have gone to Biogen. They went to us.

MR. HERPER: So, you're saying that your mass reputation may not matter, but you think you can still have a reputation within--

MR. SHKRELI: Absolutely. When I meet with companies one-on-one--I told you in the break room we're in negotiations with a major pharma company right now to acquire a drug and it hasn't hurt us one whit.

MR. HERPER: So, all this--all these negative statements are just for show, is that your--

MR. SHKRELI: Well, I mean, I think that if there's folks that--that want to make negative statements, that's up to them. But, like I said, I'm running my business and it hasn't affected.

MR. HERPER: You're also running a second business now. You bought a--shares of a company called KaloBios, and the stock surged, partly because of a short squeeze.

MR. SHKRELI: Yes.

MR. HERPER: Had you anticipated that, or was it just a play to get the short squeeze--

MR. SHKRELI: That's your perspective. My perspective is I bought 70 percent of the company, and people have made a lot of money investing on me before and people are doing it again.

MR. HERPER: Okay. Did you anticipate--it was certainly helped by the short squeeze. There were a lot of people short--

MR. SHKRELI: I--

MR. HERPER: We've all seen short squeezes.

MR. SHKRELI: You know--

MR. HERPER: There's nothing wrong with--

MR. SHKRELI: --I see some former hedge fund managers here, and I'll tell you that this phenomena of a short squeeze is probably a little more fictitious than you might think. Umm, there weren't that many people short in KaloBios before. I don't think there are that many short right now--

MR. HERPER: Just that one guy with the--

MR. SHKRELI: Yeah, the poor--the poor guy who lost his life savings betting against a company with a fabulous cancer drug. As far as I'm concerned, he deserves to lose all his money. But, you know, the--umm, you know, it's a great drug. It was run by an inept management team before. They've got a good management team now with a great track record. The company's only worth a hundred-something-million dollars. That's still cheap as far as I'm concerned.

MR. HERPER: One more. Anybody?

SPEAKER: Yes. Up here.

MR. HERPER: Okay.

MR. MILLER: Steve Miller with Express Scripts.

MR. HERPER: Ahh, good.

[Laughter.]

MR. MILLER: So, on distribution, we did support the

drug's distribution when it was $13.50--

MR. SHKRELI: So, you're talking about Express Scripts?

MR. MILLER: Yes, sir.

MR. HERPER: Yes.

MR. SHKRELI: Okay.

MR. HERPER: He's from Express Scripts.

MR. SHKRELI: Whatever. [Laughs.]

MR. MILLER: So, we supported--

MR. SHKRELI: I don't have a question for you, to be clear. I don't--I don't want you to answer anything. Do you have a question for me?

MR. MILLER: Yeah. So, we supported the drug when it was $13.50--

MR. HERPER: He gets fair response from us.

MR. SHKRELI: I--

MR. MILLER: We don't support the drug when it's $750. My question for you is, have you talked to the infectious disease--

MR. SHKRELI: I actually--

MR. MILLER: --community to see if anyone's being harmed by your new price?

MR. SHKRELI: I actually do think you guys support it, because you're not excluding our drug, are you?

MR. MILLER: No. If doctors want to use your drug--

MR. SHKRELI: So, it sounds like--so, it sounds like

you're all good.

MR. MILLER: We are all good with our dollars solution, that's true--

MR. SHKRELI: You're all good--so if I write a--if someone writes a prescription right now for Daraprim, you're still accepting it.

MR. MILLER: That's correct.

MR. SHKRELI: Awesome, man. Thanks for your business.

MR. MILLER: The--have you talked to the infectious disease communities to see if you're harming patients?

MR. SHKRELI: I have. They're thrilled that our--first time a company has ever developed a drug for toxoplasmosis, and your company--

MR. HERPER: That's not what IDSA and HIVMA are saying.

MR. SHKRELI: Well, they're not--they're not the infectious disease community. They're not even close to the infectious disease community. Meet with these guys. See what you think. I don't think you'll have a lot of respect for them at the end of your meeting. In fact, we're the first company to develop drugs for toxoplasmosis. You're the kind of company that likes to limit innovation. We're the kind of company that likes to do it, so I'm proud of what we're doing and thanks to your comment.

MR. HERPER: All right. Well, that's that.

[Laughter.]

MR. HERPER: Thanks, Martin. Thanks for coming, and, uh, we all get to go to lunch now.

MR. SHKRELI: Thanks, Matt.

MR. HERPER: Thank you.

[Applause.]

[End of recorded segment.]

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Press Release

Turing Pharmaceuticals AG Announces Appointment of Ron Tilles as Interim CEO

Zug, Switzerland, December 18, 2015 — Turing Pharmaceuticals AG, a privately-held biopharmaceutical company focused on developing and commercializing innovative treatments for serious diseases and conditions, today announced the resignation of Martin Shkreli from the position of Chief Executive Officer and the appointment of Ron Tilles to the p tion of Interim Chief Executive Officer.

Mr. Tilles will continue to serve as Chairman of the Board of Directors. He said, "We wish to thank Martin for helping us build Turing Pharmaceuticals into the dynamic research focused company it is today, and wish him the best in his future endeavors. At the same time, I am very excited about the opportunity to guide Turing Pharmaceuticals forward. We remain committed to ensuring that all patients have ready and affordable access to Daraprim and Vecamyl. Research Development on new medications continues to be a priority for the company. With the dynamic leadership of Eliseo Salinas as head of Research and Development and Nancy Retzlaff as head of Commercial Operations, Turing Pharmaceuticals is poised for great success in the coming years."

Ron Tilles has been Chairman of the Board of Directors of Turing Pharmaceuticals since the company launched late last year. Mr. Tilles began his career at Merrill Lynch in 1985 and subsequently worked with several other securities firms. Ron's experience includes numerous private equity and venture capital positions in the pharmaceutical and medical device industries c . . . the last 20 years. He earned his undergraduate degree from Middlebury College in Vermont and his Masters of Business Administration from Columbia University in New York.

About Turing

Turing Pharmaceuticals AG is a privately-held biopharmaceutical company with offices in Zug, Switzerland, and New York, New York. Turing focuses on developing and commercializing innovative treatments for serious diseases and conditions across a broad range of therapeutic areas, for which there are currently limited or no treatment options. Products being developed include intranasal ketamine for a variety of mood disorders and Syntocinon® (oxytocin nasal solution) for multiple indications. Daraprim (pyrimethamine) for the treatment of Toxoplasmosis in combination with sulfonamide and Vecamyl® (mecamylamine HCl tablets) for hypertension are Turing's first commercial products.

For more information, visit www.turingpharma.com (http://www.turingpharma.com).

Turing Pharmaceuticals AG

[redacted]

Safe Harbor

In addition to historical facts or statements of current condition, this press release contains forward-looking statements within the meaning of "Safe Harbor" provisions of The Private Securities Litigation Reform Act of 1995, including statements regarding the initiation of product development activities, including but not necessarily limited to clinical trials. Forward-looking statements provide Turing Pharmaceuticals' current expectations and forecasts of future events. Turing Pharmaceuticals' performance and financial results could differ materially from those reflected in these forward-looking statements due to general financial, economic, regulatory and political conditions affecting the biotechnology and pharmaceutical industries. Given these risks and uncertainties, any or all of these forward-looking statements may prove to be incorrect. Therefore, you should not rely on any such factors or forward-looking statements. Turing Pharmaceuticals undertakes no obligation to update publicly any forward-looking statements.

For media inquiries, please contact:

[redacted]

TURING
PHARMACEUTICALS

Martin Shkreli
[redacted]

Ron Tilles
Turing Pharmaceuticals
[redacted]

Dear Mr. Tilles,

This letter serves to confirm our discussion concerning my resignation. It was with great regret that I resigned from my role as CEO of Turing Pharmaceuticals, effective December 18, 2015.

I am grateful for having had the opportunity to serve this exceptional organization for the past year, and I offer my best wishes for its continued success.

Sincerely,

Martin Shkreli

Acknowledged & Accepted:

By:

Name: Ron Tilles

Beatrice Ehrismann TURING

Betreff:	WG: BOD Conference Call
Termin-/Besprechungsort:	Dial: [redacted] // Host Passcode: [redacted] / Participant Passcode: [redacted]
Beginn:	Mi 20.01.2016 21:30
Ende:	Mi 20.01.2016 22:30
Serientyp:	(Keine Angabe)
Besprechungsstatus:	Zugesagt
Organisation:	Deanna Green

An: Deanna Green; Ron Tilles; Martin Shkreli; Walter C. Blum

AGENDA:

1. Annulling and issuing of a share certificate (Martin Shkreli)
   Share Certificate no. 45 (330'000 shares of Martin): has to be returned to us for exchange
   New share certificate no. 45a (220'000 shares).

2. Constitution of the Board of Directors / Signatory Power dc dc

3. Appointment Signatories with joint signing authority by two:
   - Felix Berchbühl
   - Erika Maurer
   - Ged Yardy

   dc

4. Conditional capital increase
   - Public Deed of the BoD meeting dating 15.01.2016 has been notarized
   - registration is on hold until share certificate is exchanged and it is approved by phone

   dc

no additions for the time being.

Tony Clark
on hold

Protokoll der Sitzung
Minutes of the meeting

des Verwaltungsrates der
of the Board of Directors of

Turing Pharmaceuticals AG
(*Turing Pharmaceuticals Ltd*)

mit Sitz in Baar
with registered office in Baar

abgehalten am 20. Januar 2016
held on 20 January 2016

Anwesend / *Present*:

- Walter C. Blum, Vorsitzender / *Chairman of the meeting*
- Ron Tilles (telefonisch / *attending by phone*)
- Martin Shkreli (telefonisch / *attending by phone*)
- Beatrice Ehrismann (Sekretärin, Nichtmitglied / *Secretary of the meeting, non-member)*

Walter C. Blum übernimmt den Vorsitz und stellt fest, dass alle Mitglieder des Verwaltungsrates entweder physisch oder per Telefonkonferenz an der heutigen Sitzung anwesend sind und der Verwaltungsrat somit beschlussfähig ist.
Walter C. Blum takes the chair and notes that all members of the Board of Directors are either physically present or attend by way of a telephone conference at today's meeting and that accordingly the Board of Directors is quorate.

Der Verwaltungsrat der Turing Pharmaceuticals AG (nachstehend die "**Gesellschaft**") fasst einstimmig die folgenden Beschlüsse:
*The Board of Directors of Turing Pharmaceuticals Ltd (hereinafter the "**Company**") unanimously adopts the following resolutions:*

Ernennung Zeichnungsberechtigte
Appointment Signatories

Der Verwaltungsrat ernennt die nachstehenden drei Personen zu Zeichnungsberechtigten der Gesellschaft und erteilt ihnen Kollektivunterschrift zu zweien:
The Board appoints the following three persons as signatories of the company and grants joint signing authority by two:

- **Maurer, Erika**, von Schattenhalb BE, in Zürich, Zeichnungsberechtigte, mit Kollektivunterschrift zu zweien;
  ***Maurer, Erika**, citizen of Schattenhalb BE, resident in Zurich, signatory, with joint signing authority by two;*

- **Brechbühl, Felix**, von Illnau-Effretikon, in Cham, Zeichnungsberechtigter, mit Kollektivunterschrift zu zweien;
  ***Brechbühl, Felix**, citizen of Illnau-Effretikon, resident in Cham, signatory, with joint signing authority by two;*

- **Yardy, Gerald**, britischer Staatsangehöriger, in Baar, Zeichnungsberechtigter, mit Kollektivunterschrift zu zweien;
  ***Yard, Gerald**, british citizen, resident in Baar, signatory, with joint signing authority by two;*

*****

Chairman of the Meeting

Walter C. Blum

Secretary of the Meeting

Beatrice Ehrismann

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*The Board of Directors of Turing Pharmaceuticals Ltd (hereinafter the "**Company**") unanimously adopts the following resolutions:*

Konstituierung des Verwaltungsrats / Zeichnungsberechtigung
Constitution of the Board of Directors / Signatory Power

Nach den erfolgten Rücktritten von Alan Steven Geller aus dem Verwaltungsrat und von Martin Shkreli als CEO konstituiert sich der Verwaltungsrat wie folgt:
Following the resignations of Alan Steven Geller from the Board of Directors and Martin Shkreli as CEO, the Board of Directors constitutes itself as follows:

- **Tilles, Ron**, amerikanischer Staatsangehöriger, in New York (US), Präsident des Verwaltungsrates, mit Einzelunterschrift;
  ***Tilles, Ron,** American citizen, resident in New York (US), Chairman of the Board of Directors, with single signatory power;*

- **Shkreli, Martin**, amerikanischer Staatsangehöriger, in New York (US), Mitglied des Verwaltungsrates, mit Einzelunterschrift;
  ***Shkreli, Martin**, American citizen, resident in New York (US), Member of the Board of Directors, with single signatory power;*

- **Blum, Walter C.**, von Wald ZH, in Zug, Mitglied des Verwaltungsrates, mit Einzelunterschrift.
  Blum, Walter C., *from Wald ZH resident in Zug, Member of the Board of Directors, with single signatory power.*

Des Weiteren übernimmt Herr Ron Tilles ad interim die Funktion als CEO.
In addition, Mr. Ron Tilles assumes the role of interim CEO.

*****

Chairman of the Meeting

Walter C. Blum

Secretary of the Meeting

Beatrice Ehrismann

Protokoll der Sitzung
Minutes of the meeting

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*The Board of Directors of Turing Pharmaceuticals Ltd (hereinafter the "**Company**") unanimously adopts the following resolutions:*

Annullierung und Ausgabe eines Aktienzertifikats
Annulling and issuing of a share certificate

Das Aktienzertifikat Nr. 45 der Gesellschaft wurde irrtümlich über eine falsche Anzahl Aktien ausgestellt. Es soll aufgehoben und durch ein neu auszugebendes Aktienzertifikat Nr. 45a ersetzt werden:
The company's share certificate no. 45 has erroneously been issued for a wrong number of shares. It shall be annulled and replaced by a newly issued share certificate no. 45a:

Das folgende Aktienzertifikat wird aufgehoben:
The following share certificate shall be annulled:

> Nr. 45 über 330'000 Vorzugsaktien A (Namenaktien) mit einem Nennwert von je CHF 0.05, im Gesamtnennwert von CHF 16'500.--, Aktiennummern 6'632'177 - 6'962'176, ausgestellt auf Martin Shkreli;
> *No. 45 for 330,000 preference shares A (registered shares) with a nominal value of CHF 0.05 each, for a total nominal value of CHF 16,500.--, shares no. 6,632,177 - 6,962,176, issued to Martin Shkreli;*

und ersetzt durch:
and replaced by:

> Nr. 45a über 220'000 Vorzugsaktien A (Namenaktien) mit einem Nennwert von je CHF 0.05, im Gesamtnennwert von CHF 11'000.--, Aktiennummern 6'632'177 - 6'852'176, ausgestellt auf Martin Shkreli.
> *No. 45a for 220,000 preference shares A (registered shares) with a nominal value of CHF 0.05 each, for a total nominal value of CHF 11,000.--, shares no. 6,632,177 - 6,852,176, issued to Martin Shkreli.*

Der Verwaltungsrat genehmigt im Voraus die entsprechenden Änderungen des Aktienbuches.
The board of directors approves in advance the corresponding changes to the share register.

*****

Chairman of the Meeting

Walter C. Blum

Secretary of the Meeting

Beatrice Ehrismann

MARTIN SHKRELI [redacted] [redacted]

An den Verwaltungsrat der/
to the board of directors of

Turing Pharmaceuticals AG

[redacted]

New York, 10 February 2016

Rücktritt aus dem Verwaltungsrat der Turing Pharmaceuticals AG
Resignation from the Board of Directors of Turing Pharmaceuticals AG

Sehr geehrte Herren
Dear Gentlemen

Mit Bedauern erkläre ich hiermit meinen Rücktritt aus dem Verwaltungsrat der Turing Pharmaceuticals AG mit Wirkung per 10. Februar 2016. Ich bedanke mich für die mir gebotene Möglichkeit, mit Ihnen zusammenzuarbeiten.

It is with great regret that I must inform you of my decision to resign from the board of directors of Turing Pharmaceuticals Ltd effective 10 February 2016. I sincerely thank all of you for giving me the opportunity to serve together.

Freundliche Grüsse
Best regards

Martin Shkreli

** CONFIDENTIAL **

A. The fee that the distributor would charge us for the distribution, you could negotiate with them and say, you know, you should take a smaller cut.

MS. YU: Can we go off the record for a second.

MR. BRADBURY: Sure.

(Discussion off the record).

BY MS. YU:

Q. When you finalized the Daraprim transaction at Turing, did you anticipate access issues?

A. I wasn't really involved in the commercial side, so...

Q. Okay. Did you hear, you know, any discussion of any concerns about potential access issues?

A. Not that I recall.

Q. Were you aware -- are you aware that there were access issues for Daraprim?

A. During the senate hearing committee where Nancy spoke, I recall one of the senators

** CONFIDENTIAL **

mentioning something -- suggesting that, but outside of that, that was the first time --

MR. BRADBURY: That was a House hearing. Those were congressmen.

THE WITNESS: Sorry.

BY MS. YU:

Q. It's all right. Small difference. So that was a February -- in either February hearing, so you're saying in listening to that hearing, that was the first time you learned of access issues with Daraprim?

A. That's the first time I heard someone suggest that there had been.

Q. Okay. Are you aware of any action that Turing has initiated or, you know, taken to fix access issues with Daraprim?

A. So one, I'm not -- I'm not familiar with the commercial side in terms of if there are any access issues. And then -- so I'm also not aware of -- I don't have the purview into that side of this, so I don't really know what's going on.

Business Development Strategy

- **The business development team specializes in identifying and acquiring commercial assets that address unmet medical needs regardless of therapeutic area**
- **Acquire mature branded or generic products that generate stable revenue and cash flow**
- **Flexible acquisition model with a focus on a broad range of therapeutic areas**
  - Well established products with established safety and efficacy profile
  - Strong gross margins and free cash flow
  - Limited marketing and capital expenditures
- **Implement various revenue growth strategies**
  - Salesforce with a targeted commercial footprint, business intelligence and market analytics
  - High-touch closed distribution system
  - Manage regulatory affairs and supply chain
  - Improved patient advocacy and support
  - Pricing strategies

Track Record of Successful Transactions

- **Acquisition of Chenodal (chenodeoxycholic acid) and Vecamyl (mecamylamine) from Manchester Pharmaceuticals in February 2014**
  - $62.5mm total, $29.5mm upfront and $11mm in quarterly installments; 10% royalty on net sales
  - Chenodal is the standard of care for cerebrotendinous xanthomatosis (CTX)
  - Increased Chenodal price 5x with no pushback from payors
  - Hired a specialty salesforce with a targeted commercial footprint
  - Moved the product into a closed distribution to improve access and extend the product lifecycle
- **Licensing of Thiola (tiopronin) from Mission Pharmacal in May 2014**
  - $3mm upfront payment with 20% royalty on net sales
  - Thiola is indicated for the prevention of cystine stone formation in patients with cystinuria
  - Increased price 21x with no pushback from payors
  - Restored drug shortage issues and increased volumes significantly
  - Moved the product into a closed distribution to improve access and extend the product lifecycle
  - Hired a specialty salesforce with a targeted commercial footprint
- Acquisition of Daraprim (pyrimethamine) from Impax Laboratories in August 2015
  - $55mm upfront payment
  - Daraprim is indicated for the treatment of toxoplasmosis
  - Increased price 43x with no pushback from payors
  - Hired a specialty salesforce with a targeted commercial footprint

Case Study: Thiola (tiopronin)

- **Key executives at Turing Pharmaceuticals were responsible for the licensing of Thiola at Retrophin from Mission Pharmacal in May 2014**
  - $3mm upfront payment with 20% royalty on net sales
  - Asset TTM revenue before the license was $1.6mm
  - Drug shortage and less than 300 patients on drug prior to the license
- **Thiola is indicated for the prevention of cystine (kidney) stone formation in patients with cystinuria**
  - Standard of care in niche orphan kidney indication
- **Significant revenue growth driven by increases in price and volume**
  - Increased price 21x with no pushback from payors
  - Hired a specialty salesforce with a targeted commercial footprint
  - Restored the supply chain
  - Improved patient advocacy and support
  - Moved the product into a closed distribution to improve access and extend the product lifecycle
- **Currently, over 700 patients on therapy with plans to increase to over 1,000 patients by the end of the year 2015**
  - Implies around $60mm in revenue with greater than $80mm revenue by the end of the year

Multiple Accretive Acquisitions in the Pipeline

- **Over 10 potential acquisitions in the pipeline at various stages of negotiation with counterparties**
  - Strong cash flows
  - Acquiring targets at attractive multiples
- **Standard of care commercial asset for a life threatening indication**
  - <$50mm in revenue
  - Ability to extend life cycle by developing modified formulations and developing analogues
  - No salesforce currently
  - Product not priced appropriately with opportunity to increase >20x
  - No generics
- **Commercial asset for a mass market indication with limited treatment options**
  - >$50mm in revenue
  - Currently low brand awareness amongst patients and physicians
  - Ability to extend life cycle by developing modified formulations
  - No salesforce currently
  - Product not priced appropriately with opportunity to increase >2x
  - No generics

Drug Pricing

- Drugs are typically non-discretionary and consumers are relatively price insensitive
- Typically there's an inverse correlation between prevalence of a disease and the annual cost of treatment
- Exclusivity (closed distribution) creates a barrier and pricing power

Spec pharma deals that have resulted in significant immediate price increases on acquired products

Acquirer	Target	Date of deal announcement	Date of deal close	Product	Price increases between deal announcement and deal close	Date of price increase	Price increases within 6 months post deal close	Date of price increase
AXRX	HITK	8/27/2013	4/17/2014	Acyclovir Oral Suspension	40%	9/25/2013	226%	9/4/2014
				Albuterol Sulfate Inhalation Nebulization Soluti				
				Clobetasol Propionate E External Cream			673%	8/8/2014
				Clobetasol Propionate External Cream			1732%	8/8/2014
				Clobetasol Propionate External Gel			1387%	8/8/2014
				Clobetasol Propionate External Ointment			2121%	8/8/2014
				Clobetasol Propionate External Solution			568%	8/8/2014
				Lidocaine-Prilocaine External Cream			23%	8/8/2014
				Ofloxacin Ophthalmic Solution			387%	8/13/2014
ENDP	AUXL	10/9/2014	1/29/2015	Stendra	9%	1/1/2015		
				Testim	10%	1/1/2015		
MNK	CADX	2/11/2014	3/13/2014	Ofirmev			140%	5/15/2014
SLXP	SNTS	8/11/2013	1/2/2014	Glumetza			15%	6/3/2014
				Fenoglide			10%	6/3/2014
VRX	Marathon		2/14/2015	Amytal	8%	2/6/2014		
				Ipriva			50%	2/20/2015
				Isuprel			500%	2/10/2015
				Nitropress			200%	2/10/2015
				Pepcid (famotidine			200%	2/20/2015
				Seconal			100%	2/20/2015
VRX	SLXP	2/22/2015	4/1/2015	Aprisc			50%	4/1/2015
				Cydoset	20%	3/1/2015		
				Fenoglide			200%	4/1/2015
				Ucerls	10%	3/13/2015		
				Xifaxan 550 mg	9%	3/25/2015		
				Metaxaly			399%	4/1/2015

Source: Goldman Sachs Global Company data, Goldman Sachs Global Investment Research, Medispan

NOTE: THIS DEPOSITION IS A SEALED EXHIBIT

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NOTE: THIS DEPOSITION IS A SEALED EXHIBIT

From: Martin Shkreli
To: Martin Shkreli
BCC: Sandeep@[redacted]; Sam@[redacted]; DM@[redacted]; Keith.Manchester[redacted]; Oren.Eisner[redacted]; sboyd@[redacted]; gregrea[redacted]; DChan@[redacted]; jim[redacted]; agtrading5[redacted]; gwhaywood642[redacted]; ken@[redacted]; edmund.j.sullivan[redacted]; pedro.pangea@[redacted]; daniel.m.tasse@[redacted]; Leonora@[redacted]; danielshamoon17@[redacted]; gzaffiro@[redacted]; simon.berring@[redacted]; ZanFleming@[redacted]; ddeman@[redacted]; Ron Tilles ([redacted]; Kevin Mulleady [redacted]; Eliseo Salinas [redacted]; Edwin Urrutia [redacted]; Michael Harrison ([redacted]; Michael Smith [redacted]; Patrick Crutcher [redacted]; Megan Roberts; Ed Painter; Stephen Thomas [redacted]; Robert Hofbauer; Nick Pelliccione [redacted]; Kristen Lewis [redacted]; Chris Lau [redacted]; Tashdid Hasan [redacted]; Keller Perry [redacted]; Peter Myall [redacted]; Nancy Retzlaff [redacted]; Catherine Chen ([redacted]; Christopher Thorn [redacted]
Sent: 11/10/2015 11:48:49 AM
Subject: RE: Weekly Investor Update

Dear Investor,

Last week we sold 34 bottles to the important Walgreens channel, up from 23 last week, which we skipped reporting. I am very pleased with this demand and will again highlight the superb operational and management skills of our Chief Commercial Officer, Nancy Retzlaff. This level of demand represents approximately $130 million in revenue run-rate.

We look forward to eventual removal of the retail channel, which if it converted to our Walgreens channel, would represent an approximate doubling in our revenue. As always, you can contact me with any questions.

Martin Shkreli
Founder & CEO
Turing Pharmaceuticals AG
[redacted]

Daraprim Walgreens Weekly Bottles

8/14/2015	8/21/2015	8/28/2015	9/4/2015	9/11/2015	9/18/2015	9/25/2015	10/2/2015	10/9/2015	10/16/2015	10/23/2015	10/30/2015	11/6/2015
Week 33	Week 34	Week 35	Week 36	Week 37	Week 38	Week 39	Week 40	Week 41	Week 42	Week 43	Week 44	Week 45
14	11	18	19	14	29	25	23	29	25	36	23	34

From: Michael Smith
To: Patrick Crutcher; Edwin Urrutia
Sent: 8/14/2015 10:25:08 AM
Subject: RE: Sulfa/Pyr Market Research
Attachments: Project Stereo Forecast.xlsx; Project Stereo Market Research.pdf

After reading thru the deck again, it seems fine as is. I've attached my basic model. Kurt said he'll finish the opinion this afternoon.

From: Tina Ghorban
Sent: Friday, August 14, 2015 8:51 AM
To: Michael Smith [redacted] Patrick Crutcher [redacted]
Edwin Urrutia [redacted]
Cc: Nancy Retzlaff [redacted]
Subject: RE: Sulfa/Pyr Market Research

Yes, but it's a big file.

From: Michael Smith
Sent: Friday, August 14, 2015 8:48 AM
To: Tina Ghorban [redacted]; Patrick Crutcher [redacted], Edwin Urrutia [redacted]
Cc: Nancy Retzlaff [redacted]
Subject: RE: Sulfa/Pyr Market Research

Do you have this in .pptx?

From: Tina Ghorban
Sent: Thursday, August 13, 2015 1:32 PM
To: Michael Smith [redacted] Patrick Crutcher [redacted] Edwin Urrutia [redacted]
Cc: Nancy Retzlaff [redacted]>
Subject: Sulfa/Pyr Market Research

Let me know if this works for the market research. I can take the date off and make other changes to customize for the Sandoz audience.

Tina Ghorban
Senior Director
Business Analytics & Customer Insights

Turing Pharmaceuticals
[redacted]>

TURING
PHARMACEUTICALS

Market Assessment for
Sulfadiazine And Pyrimethamine

July 7, 2015

Objectives and Methodology

Business Objective:

- Evaluate the potential to preserve the value of sulfadiazine and/or pyrimethamine for the treatment of toxoplasmosis in the event of an increase in the cost of these agents.

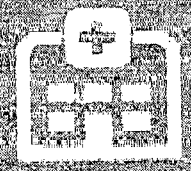
Research Objectives:

- Clarify the toxoplasmosis treatment algorithm and considerations in selecting therapies
- Identify differences in approach for specific patient sub-populations
- Determine the impact of cost on treatment decisions by sub-population
- Explore opportunities to enhance the value of sulfadiazine and/or pyrimethamine in the treatment of toxoplasmosis, *e.g.* lifecycle strategies and partnerships

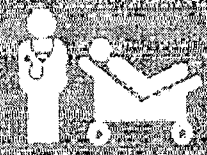
Physician Telephone Depth Interviews - May 20, 21, 22, 2015

Infectious Disease	Pediatric Infectious Disease	PCP's	Internal Medicine	OB/GYN	TOTAL
7	1	2	5	2	17

Typical Toxoplasmosis Treatment Flow



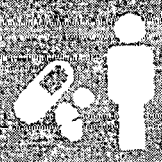
Patient presents with acute symptoms (CNS abnormality, seizures, abnormality of gait) to ER or regular PCP/IM/ID



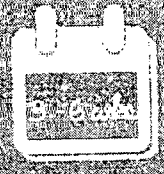
Patient is admitted to the hospital in the care of an ID for brain imaging

ID Rx's S+P and possibly IV steroids

- If sulfa allergy, substitute clinda
- If clinda intolerable, substitute atoquavone, Dapsone, or Zithromax

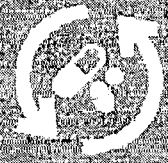


Discharge on oral S+P, or possibly switch to Bactrim for cost and convenience

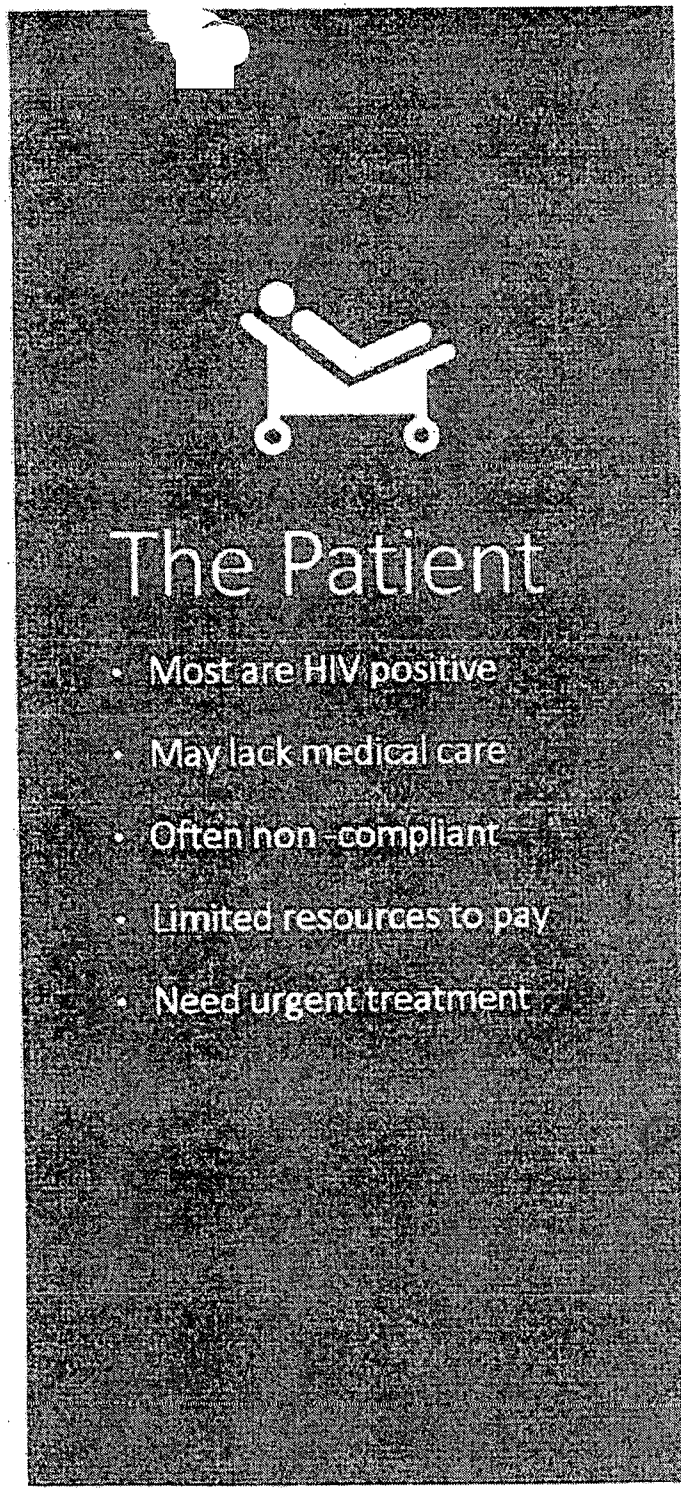


Acute treatment usually lasts for 3-6 weeks

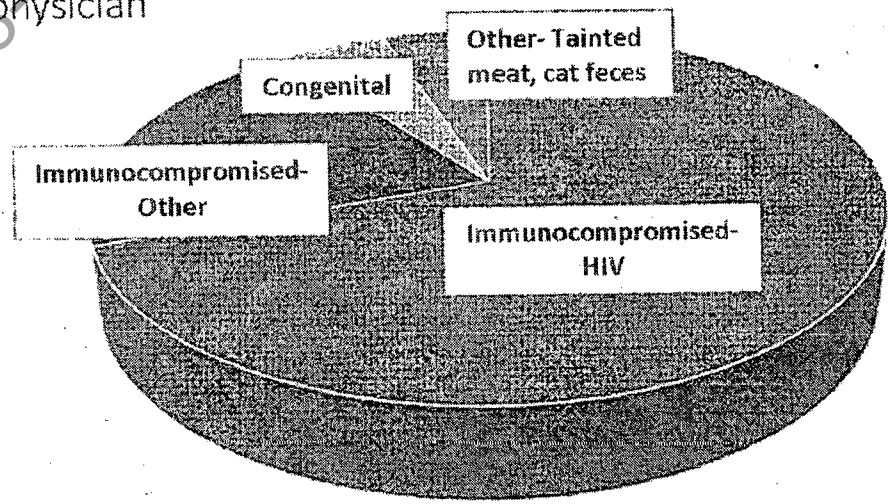
- If sulfa allergy, substitute clinda
- If S+P not well reimbursed, substitute Bactrim

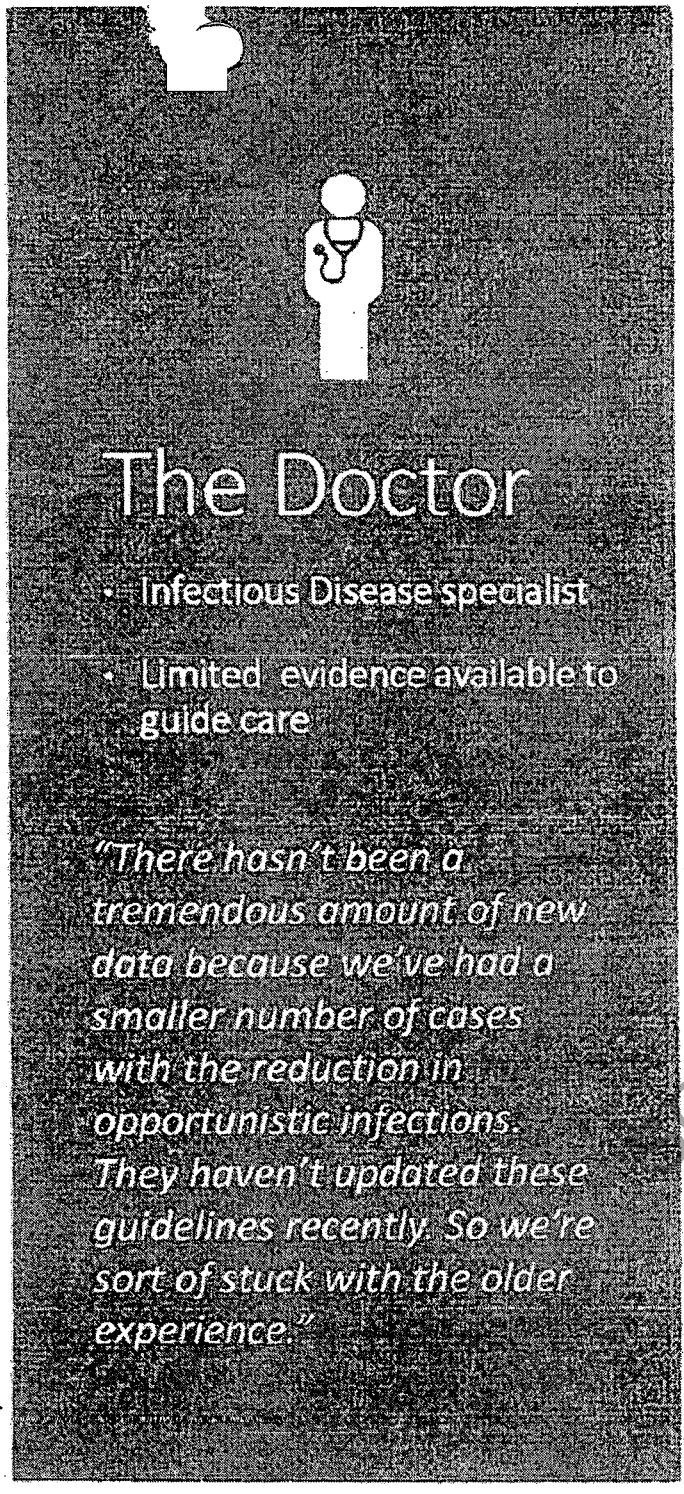


Bactrim for ongoing maintenance as necessary (for convenience, cost and protects against pneumocystis pneumonia and nocardia), usually until CD4 > 200 for > 6 months

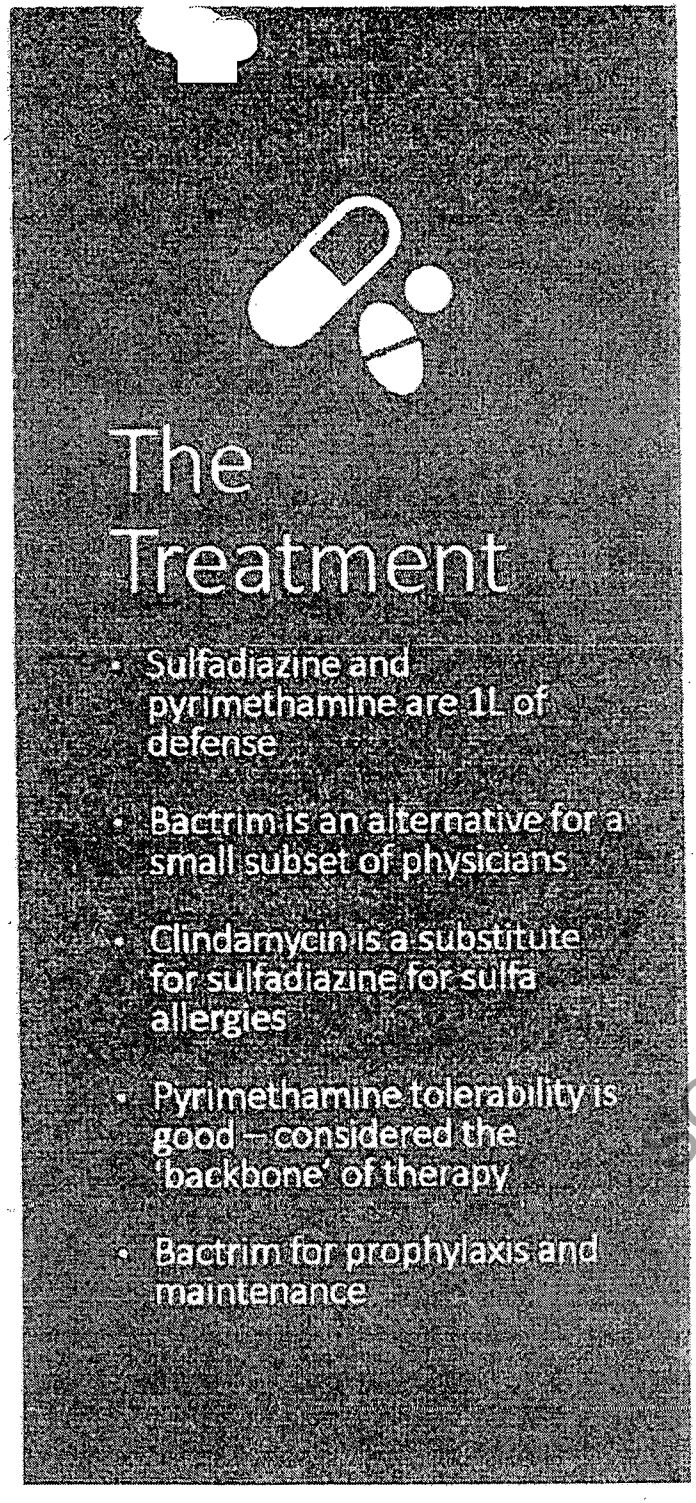


- The majority of toxoplasmosis (toxo) cases are seen in HIV-infected patients. In many cases, these are patients who:
  - Have not sought regular medical care with the result that diagnosis and treatment of HIV and opportunistic infections may have been delayed
  - Struggle to comply with long-term and/or complex preventive medication regimens
  - Have limited ability to pay for treatment
- Incidence is perceived to be decreasing as improved HIV treatments have resulted in relatively stable immunity today
- The need to treat is considered urgent in all types of cases with the goal of stabilizing disease, not eradicating it
- Treatment is often initiated in-hospital
  - Patients may present with acute symptoms at the ER or be immediately recommended for admission by their outpatient physician

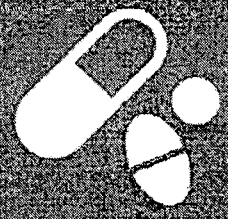




- Treatment is most commonly initiated by infectious disease specialists (IDs) in both the inpatient and outpatient settings
  - PCPs, IMs, and OB/Gyns typically refer to an infectious disease specialist (ID) when a diagnosis is suspected or confirmed via imaging studies, PCR testing, or IgG and IgM testing
  - Other physicians may be involved in co-management and monitoring, especially during the maintenance phase of therapy
- Poor clinical evidence is available to guide treatment of toxo; most physicians reference CDC, NIH and IDSA guidelines for managing toxo in HIV patients, expert opinion, and personal experience
  - With fewer opportunistic infections in the population, newer treatments are not being developed, and guidelines have not been updated or amended to address non-HIV populations



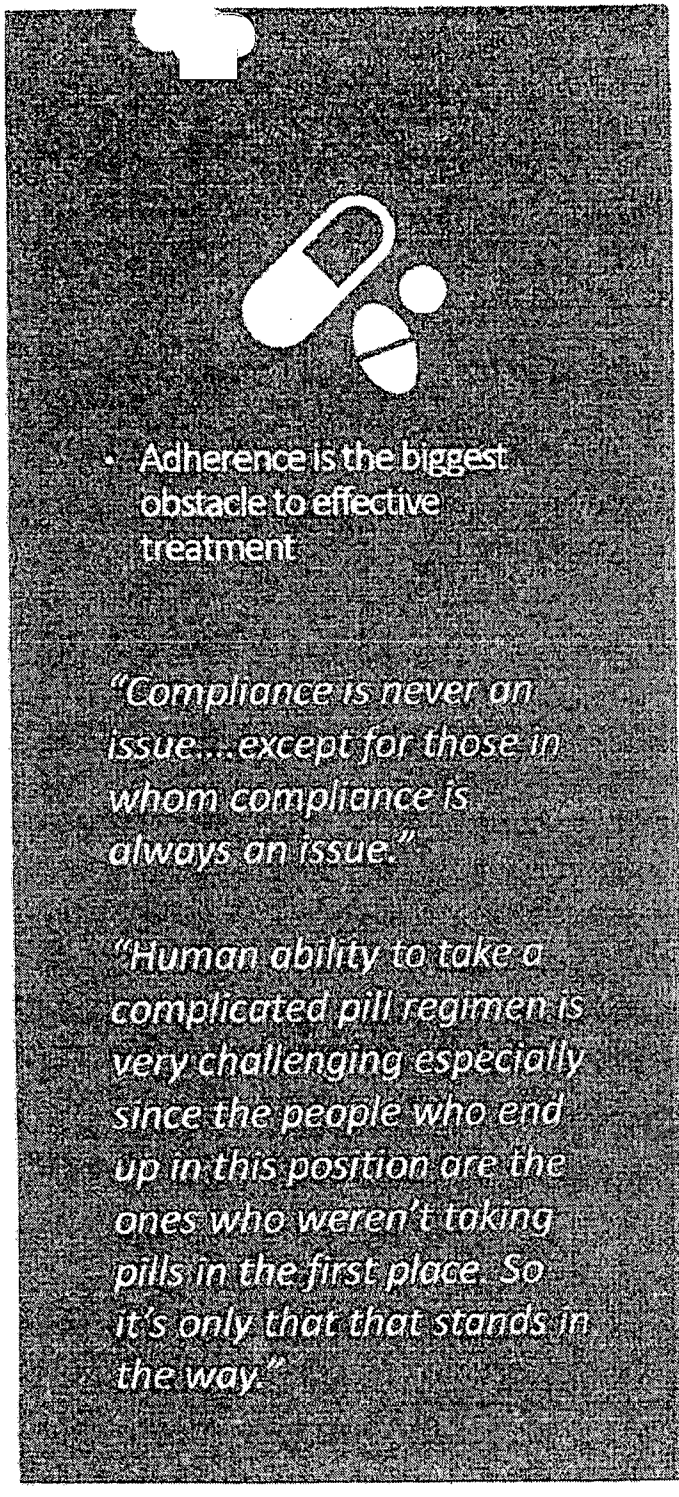
- Regardless of the treatment setting, nearly all physicians prescribe sulfadiazine and pyrimethamine 1L for all types of toxo cases
  - Response is often seen in 2-3 weeks
  - For HIV patients, acute treatment usually lasts 3-6 weeks
  - Bactrim is an alternative 1L treatment for a very small subset of physicians who may tend to be younger and prefer the simplicity and cost advantages of a combination pill
- Clindamycin is the primary substitute for sulfadiazine in patients exhibiting a sulfa allergy
- Pyrimethamine tolerability is good, and side effects are rarely observed; thus it is a "backbone" of therapy and not often substituted
- Bactrim is preferred for prophylaxis in HIV patients and as maintenance therapy in all patients who require it
  - Fixed dose combination supports compliance and is relatively inexpensive – both important for long-term use



- Bactrim owns maintenance treatment and prophylactic therapy

"While we would like to follow guidelines and be able to give them the best care possible, sometimes it needs compromising the gold standard treatment with something you think is going to be more tolerable, namely monotherapy for simplicity."

- After the acute phase of toxo treatment (3-6 weeks), HIV patients are routinely transitioned to Bactrim for maintenance, sometimes even before full treatment regimen of sulfadiazine and pyrimethamine is complete
  - Convenient combination regimen is inexpensive and straightforward relative to sulfadiazine and pyrimethamine
  - Broad spectrum antibiotic protects against other opportunistic infections (pneumocystis pneumonia)
  - HIV patients will continue until CD4 count is >200 for at least six months and possibly for a lifetime
- Post-acute therapy for non-HIV patients is lower doses of sulfadiazine and pyrimethamine or therapy may be discontinued depending on clinical and radiologic evidence of remission/ongoing disease
- Bactrim is also commonly used as prophylactic therapy to prevent pneumocystis pneumonia in HIV patients with CD4 counts < 200
  - Prevention of toxo is a side benefit; *"two birds with one stone"*



- Adherence is the biggest obstacle to effective treatment

"Compliance is never an issue…except for those in whom compliance is always an issue."

"Human ability to take a complicated pill regimen is very challenging especially since the people who end up in this position are the ones who weren't taking pills in the first place. So it's only that that stands in the way."

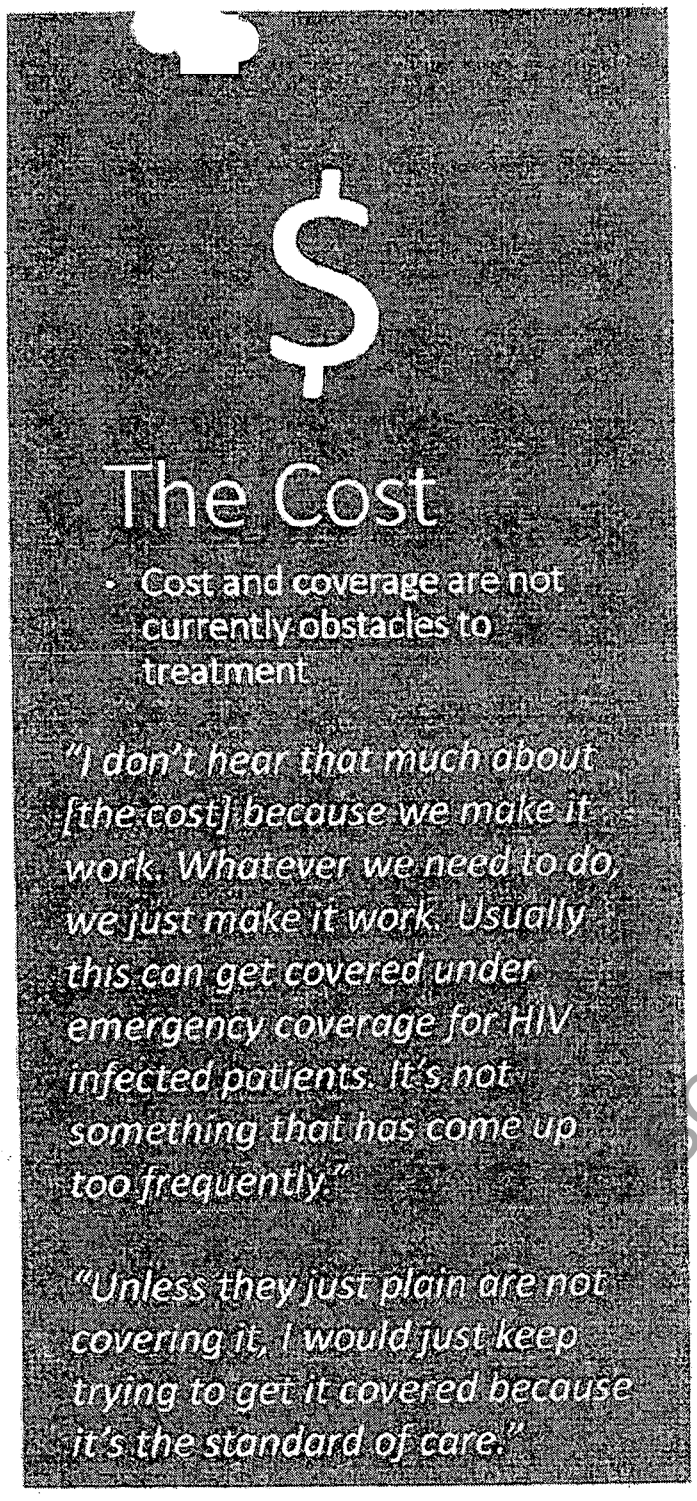
- Sulfadiazine + pyrimethamine comprises a difficult regimen, especially for HIV patients taking multiple medications.
- "Medication exhaustion" stems from:
  - A frequent and complicated dosing regimen
    - Sulfadiazine is QID, Pyrimethamine is TID
  - Difficulty swallowing multiple or large pills
  - Coping with side effects

The most challenging cases tend to be those where diagnosis and treatment of HIV and opportunistic infections have been delayed, and compliance with preventive medications has been poor.

These factors may be compounded by a history of substance abuse and other psychosocial problems and poor socioeconomic circumstances.

For these patients in particular, strategies to support compliance and adherence are critical.

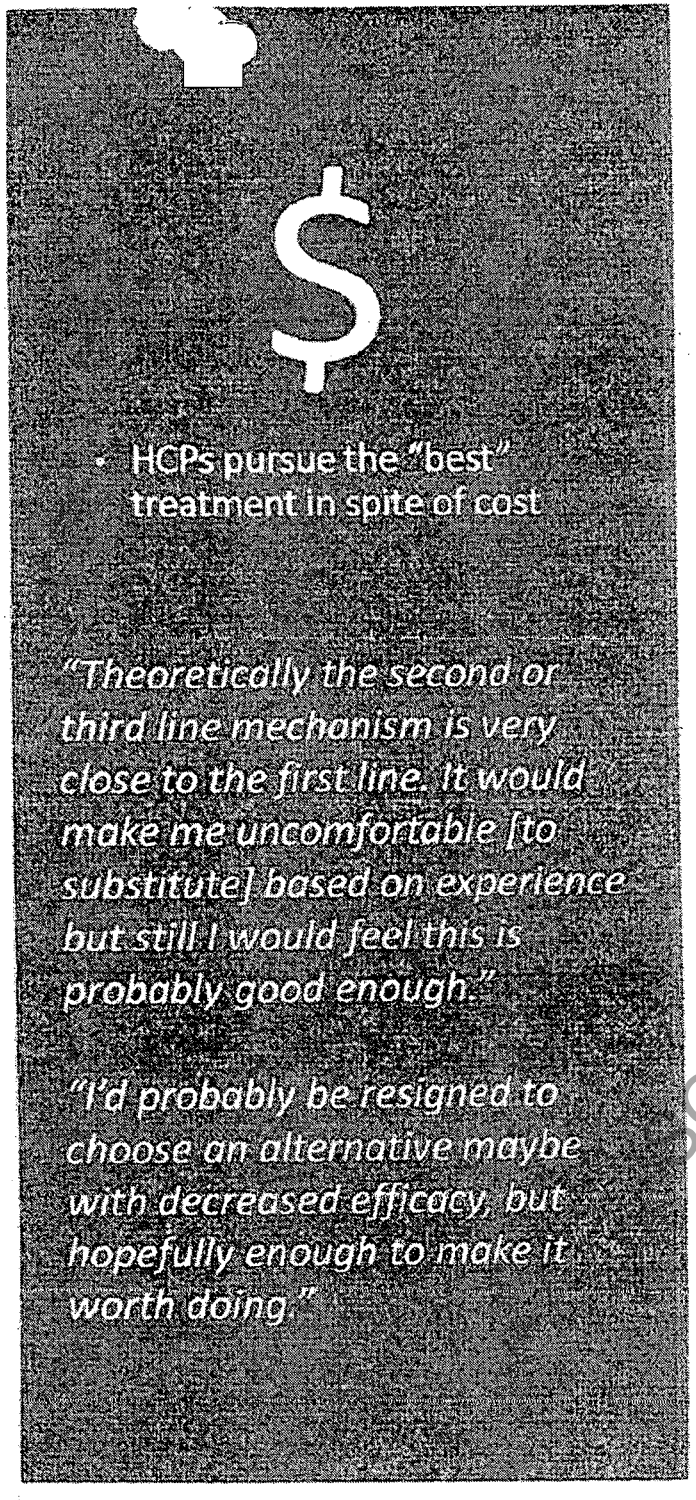
"It's highly diverse, but when patients have toxo, they're usually tougher patients where they're late to care. Sometimes they're suffering from housing needs. Sometimes they're suffering from mental health or substance abuse."



COST CHALLENGES

- Physicians do not report high out-of-pocket costs, required prior authorizations, or other access barriers to toxo medications
- The standard toxo treatments are perceived to be affordable
  - Sulfa is thought to be relatively expensive, and Bactrim is inexpensive
- Physicians would prefer not to have to substitute another drug for sulfadiazine and pyrimethamine due to cost
  - Most physicians would complete prior authorizations or pursue financial support in the interest of securing "gold standard" treatment for patients

For Medicaid beneficiaries, toxo drugs may be free
- KFF reports that Medicaid covers half of all people with HIV in the country (March 2013)
- ADAP coverage mentioned as well



TRADE-OFFS

- If patients were to decline the "best" therapy due to cost, physicians would reluctantly prescribe their second line alternative to sulfadiazine
  - Some would expect and accept decreased efficacy, as suboptimal therapy would be better than no therapy
  - A few admitted that they "wouldn't lose sleep" over having to make the substitution
- Physicians would prefer not to have to substitute another drug for sulfadiazine or pyrimethamine and would complete prior authorizations or pursue financial support in the interest of securing "gold standard" treatment
  - Some would press patients to accept a higher cost in the interest of the best care
  - Some would explain the potential risk of a compromised outcome, especially in cases of severe neurological impairment
- Physicians are at a loss to think of an appropriate alternative to pyrimethamine
  - Second line regimens are based on pyrimethamine, the "backbone" of therapy
  - Might consult the literature or experts
  - A few mention atovaquone and Bactrim as possible substitutes

The Opportunity

- Compliance and adherence are the biggest barriers to effective treatment
- New formulations could address unmet needs
- Adding to the body of clinical evidence also helpful

"If there is a way to reduce the frequency, number of pills, and the simplicity of the regimen, there is the best chance of success."

- Fixed dose combinations of sulfadiazine and pyrimethamine are a *"no brainer"* to help improve compliance
  - Multiple combinations would be required for acute versus maintenance dosages and to accommodate differences in the recommended dosing frequency of each
  - Pill size may be an issue
  - Extended release formulations (*e.g.*, one injection per month) would also address compliance issues
- Sulfadiazine and pyrimethamine in an IV formulation could be useful for NPO patients in-hospital
- Resources/services to support medication adherence could be useful, especially those that utilize technology, *e.g.* a digital monitoring device on pill bottle cap
- New Level I evidence about optimal treatment of toxo is needed, especially head-to-head studies, but it may be extremely difficult to enroll appropriate populations in numbers sufficient for randomized control trials

Patient Needs

Conclusion

Patient compliance is the biggest obstacle to effective treatment

- Compliance with a complicated regimen
- Adherence over a long period, possibly a lifetime
- Long term out-of-pocket expense

Recommendation

Make the regimen easier for compliance

- Medication reminder platform
- New formulations and packaging, *e.g.* combination pills, extended release formulations, combination blister packs, IV formulations, etc.

Support for the Standard of Care

Conclusion

Although current guidelines are clear, evidence supporting pyrimethamine + sulfadiazine is limited

- Currently limited to HIV primarily
- All physicians, and IDs in particular, value clinical data and would be receptive to new information

Recommendation

Deepen ID commitment to the standard of care

- Invest in a retrospective analysis of cases or an expert panel review regarding toxo treatment and outcomes in HIV and other affected populations

Cost Perception

Conclusion

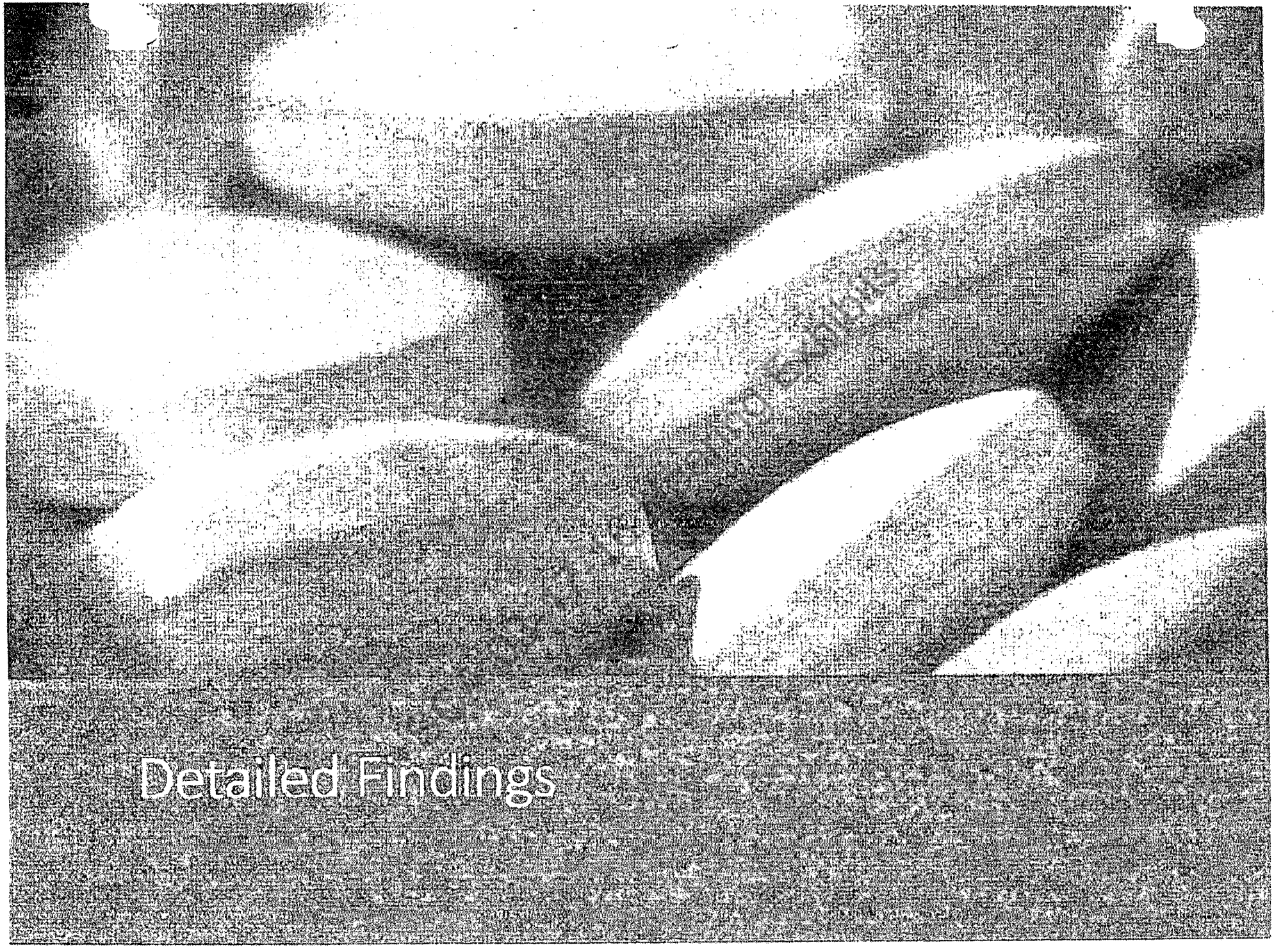
As the clinicians primarily responsible for toxo treatment, IDs are not particularly cost- or price-sensitive

- Highly focused on therapeutic benefit
- Think current cost of pyrimethamine + sulfadiazine is more expensive than other 2L therapies already but consider it the gold standard nonetheless
- Will take action to secure "best" treatment for patients

Recommendation

Enhance the pyrimethamine + sulfadiazine value proposition and offset perceptions of high cost

- Make the regimen affordable with a Patient Assistance Program for patients unable to pay


Detailed Findings

TREATMENT ENVIRONMENT

TURING

Incidence is decreasing but treating toxoplasmosis is an urgent matter

"It's challenging because it's not only one thing, the parasite. It's also the immune response. And each person is different. So you have a factor here you can't really control and standardize between patients: the host response to the parasite. That makes it very complicated."

- The vast majority of toxoplasmosis cases are seen in HIV-infected patients, followed by (in order of frequency of mentions):
  - Other immunocompromised patients such as transplant patients and patients on chemotherapy
  - Retinitis
  - Immunocompetent patients
  - Congenital
  - Pregnancy
- Incidence is perceived to be decreasing as improved antiretroviral therapy and widespread use of Bactrim as prophylaxis (in HIV patients with CD4 counts <200) result in relatively stable immunity today
- The need to treat is considered urgent in all types of cases, and treatment is often initiated in-hospital
- Goals of treatment are stability and control, not eradication, as disease often recurs

Infectious Disease specialists lead treatment and the clinical team

- Patients experiencing serious symptoms may present in the ER or be immediately recommended for admission by their outpatient physician
- PCPs, IMs, and ob/gyns typically refer to an infectious disease specialist (ID) when a diagnosis is suspected or confirmed via imaging studies, PCR testing, or IgG and IgM testing
- Treatment is most commonly initiated by infectious disease specialists (IDs) in both the inpatient and outpatient settings
  - Other physicians may be involved in co-management and monitoring, especially during the maintenance phase of therapy

Sulfadiazine and pyrimethamine are the first line standard for acute care

"There hasn't been a tremendous amount of new data because we've had a smaller number of cases with the reduction in opportunistic infections. They haven't updated these guidelines recently. So we're sort of stuck with the older experience."

- Regardless of the treatment setting, nearly all physicians prescribe sulfadiazine and pyrimethamine for all acute patients
  - Consistent with CDC and NIH guidelines for managing toxo in HIV patients which are generalized to other populations
  - Bactrim is an alternative first line treatment for a very small subset of physicians who may tend to be younger and prefer the simplicity and cost advantages of a combination pill
  - Leucovorin is used concomitantly in HIV patients
  - Although not commercially available in the U.S., spiramycin is recommended for infected women <18 weeks into their pregnancy, and S+P is recommended for infected women >18 weeks into their pregnancy
  - For congenital cases, S+P or Bactrim may be used
- Many perceive S+P to offer efficacy superior to other options but physicians acknowledge limited Level I evidence is available
- Perception is that sulfadiazine may be delivered intravenously to inpatients (although an IV formulation is not commercially available); patients are discharged with prescriptions for oral S+P
- Patients are typically treated with S+P for 3-6 weeks, when symptoms may be lessened or resolved and/or imaging reveals brain and/or eye lesions have shrunk in size

Clindamycin dominates 2L treatment after sulfadiazine but some use other options

- For patients exhibiting a sulfa allergy or side effects, clindamycin is the primary second line treatment substituted for sulfadiazine
  - Although clinical evidence is poor, clinda thought to offer efficacy inferior to sulfadiazine despite patients progressing well on it
- Pyrimethamine is generally well-tolerated, and substitutions do not appear to be necessary
- Second or third line alternatives to S, especially in those who don't tolerate clinda or do not respond to treatment, include:
  - Atoquavone
  - Dapsone
  - Zithromax
  - Possibly high dose Bactrim

Bactrim owns maintenance treatment and prophylactic therapy

"While we would like to follow guidelines and be able to give them the best care possible, sometimes it needs compromising the gold standard treatment with something you think is going to be more tolerable, namely monotherapy for simplicity."

- After the acute phase of toxo treatment, HIV patients are routinely transitioned to Bactrim for maintenance, sometimes even before full treatment regimen of S+P is complete
  - Convenient combination regimen is inexpensive and straightforward relative to S+P
  - Broad spectrum antibiotic protects against other opportunistic infections
  - HIV patients will continue until CD4 counts are >200 for at least six months and possibly for a lifetime
- Post-acute therapy for non-HIV patients is lower doses of S+P or therapy may be discontinued depending on clinical and radiologic evidence of remission/ongoing disease
- Bactrim is commonly used as prophylactic therapy to prevent pneumocystis pneumonia in HIV patients with CD4 counts < 200
  - Prevention of toxo is a side benefit; *"two birds with one stone"*

Adherence is the biggest obstacle to effective treatment

"Compliance is never an issue...except for those in whom compliance is always an issue."

"Human ability to take a complicated pill regimen is very challenging especially since the people who end up in this position are the ones who weren't taking pills in the first place. So it's only that that stands in the way."

- S+P comprises a difficult regimen, especially for HIV patients taking multiple medications.
- "Medication exhaustion" stems from:
  - A frequent and complicated dosing regimen
    - S is QID, P is TID
  - Difficulty swallowing multiple or large pills
  - Coping with side effects

The most challenging cases tend to be those where diagnosis and treatment of HIV and opportunistic infections have been delayed, and compliance with preventive medications has been poor.

These factors may be compounded by a history of substance abuse and other psychosocial problems and poor socioeconomic circumstances.

For these patients in particular, strategies to support compliance and adherence are critical.

"It's highly diverse, but when patients have toxo, they're usually tougher patients where they're late to care. Sometimes they're suffering from housing needs. Sometimes they're suffering from mental health or substance abuse."

COST CHALLENGES AND TRADE-OFFS

TURING

Cost and coverage are not obstacles to treatment today

"I don't hear that much about it because we make it work. Whatever we need to do, we just make it work. Usually this can get covered under emergency coverage for HIV infected patients. It's not something that has come up too frequently."

- Physicians do not report high out-of-pocket costs, required prior authorizations, or other access barriers to toxo medications
- The standard toxo treatments are perceived to be affordable but sulfa is thought to be relatively expensive, and Bactrim is inexpensive

For Medicaid beneficiaries, toxo drugs may be free

- The Kaiser Family Foundation reports that Medicaid covers half of all people with HIV in the country (March 2013)
- In this study, physician estimates for their patients covered by Medicaid range from <10% to 70
- ADAP coverage mentioned as well

HCPs pursue the "best" treatment in spite of cost

"Unless they just plain are not covering it, I would just keep trying to get it covered because it's the standard of care."

"Theoretically the second or third line mechanism is very close to the first line. It would make me uncomfortable [to substitute] based on experience but still I would feel this is probably good enough."

"I'd probably be resigned to choose an alternative maybe with decreased efficacy, but hopefully enough to make it worth doing."

- Physicians would prefer not to have to substitute another drug for S or P and would complete prior authorizations or pursue financial support in the interest of securing "gold standard" treatment
  - Some would press patients to accept a higher cost in the interest of the best care
  - Some would explain the potential risk of a compromised outcome, especially in cases of severe neurological impairment
- If patients were to decline the "best" therapy due to cost, physicians would reluctantly prescribe their second line alternative to S
  - Some would expect and accept decreased efficacy, as suboptimal therapy would be better than no therapy
  - A few admitted that they "wouldn't lose sleep" over having to make the substitution
- Physicians are at a loss to think of an appropriate alternative to P
  - Second line regimens are based on P, the "backbone" of therapy
  - Might consult the literature or experts
  - A few mention atovaquone and Bactrim as possible substitutes

Patient advocacy organizations do not influence physician behavior

- Although they may be peripherally aware of lobbying and public relations initiatives, physicians are not themselves directly involved with patient advocacy organizations
  - More likely to participate in advocacy via their own professional societies
- In cases where they disprove of industry or individual manufacturers, physicians continue to pursue the "best" therapeutic option for patients, especially in potentially life-threatening situations
- Many feel the number of toxoplasmosis patients is too small to stimulate a significant lobbying effort were the cost of therapy to become an issue

OPPORTUNITIES AND UNMET NEEDS

TURING

New forms of S+P generate modest interest

"If there is a way to reduce the frequency, number of pills, and the simplicity of the regimen, there is the best chance of success."

- Potential new formulations of S and P are a "no brainer" to improve compliance and adherence but are not a factor in whether the drugs will be used or used more
  - Multiple fixed dose combinations of S + P would be required to support acute versus maintenance dosages and differences in the recommended dosing frequency of each
    - A combination pill can't be too large
    - One recommendation: Sulfa 2000 mg/pyrim 25 mg BID and sulfa 1000 mg/pyrim 12.5 mg BID
- While P and Bactrim are both available in IV formulations for inpatient use, sulfadiazine is not which could be useful for NPO patients
- Extended release forms of drugs may also support adherence, *e.g.* an injectable formulation that is active for 1-3 months
- Packaging S and P together may also help patients, e.g. blister packs that make the regimen visually obvious and convenient

Limited evidence supports the standard of care but new studies pose recruiting challenge

- Level I evidence regarding treatment of toxo is lacking and there may be opportunities to expand what is known about:
  - CNS-related outcomes
  - Quality of life
  - Survival
- Head-to-head studies are of interest but it would be extremely difficult to enroll appropriate populations in numbers sufficient for randomized control trials
  - Interest in a non-inferiority trial of S+P versus Bactrim: can a less expensive therapy be substituted for the standard of care?

Support for medication adherence is relevant and important in toxoplasmosis

- Seriously ill patients being discharged from hospital or treated on an outpatient basis often have access to support
  - *E.g.* transportation services, home-based care, an assigned case worker/social worker, Medication Therapy Management services, etc.
- Additional resources to support medication adherence specifically could be useful, especially those that utilize technology:
  - Text-based medication reminders
  - Chip/reader attached to bottle cap to track and monitor compliance
  - Inbound and outbound telephonic support to patients (focused on adherence and managing side effects)
  - Visual aids to educate and remind about the treatment regimen
  - Support groups

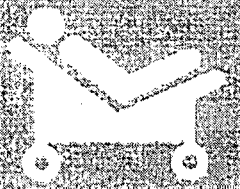
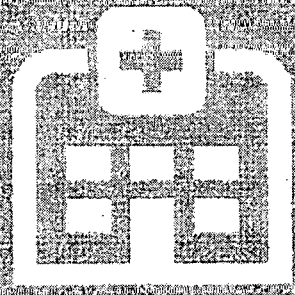
APPENDIX

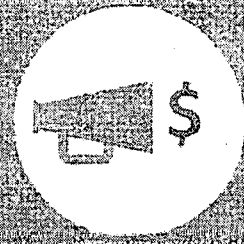
TURING

Screener

Discussion Guide

Toxoplasmosis Treatment Context



Most patients with HIV presenting with CNS toxo are often (>90%) hospitalized for parenteral antimicrobial treatment

Typically, presentation is to the hospital ER where they are admitted

All patients referred to Infectious Disease (ID) specialist

IDs will advocate for the standard of care even if it is costly

is the largest barrier to treatment

TURING