GILEAD

MEMO

CONFIDENTIAL

To:	Development Committee
Cc:	Mark Bosse; Jung Choi
From:	Peter Virsik
Date:	September 18, 2003
Re:	**Financial Analysis of GS7340 as a Tenofovir Exclusivity Extension**

Summary

Gilead is currently developing GS7340 as a next generation prodrug of tenofovir for the treatment of HIV. While the product profile of GS7340 is not yet solidified, GS7340 may provide an additional four years of market exclusivity compared to tenofovir disoproxil fumarate (TDF). The following financial analysis assumes that Gilead will develop GS7340 to replace both Viread and the TDF/FTC combination product in order to extend the exclusivity of the tenofovir franchise by four years. We have assumed a product profile for GS7340 that is incrementally improved from TDF with respect to antiviral potency. Based upon this analysis, we conclude that developing GS7340 as an exclusivity extension strategy can provide a positive financial return provided that at least 85,000 patients in the US and EU are switched to GS7340 before TDF's patent expiration and are maintained on therapy through 2021 (roughly $325MM in yearly Net Sales). A historical analysis, key assumptions, and a summary of the financial results are presented in this memo.

Case Studies of Patent Expiration and Product Extension Strategies

Previous examples of product exclusivity expiration were examined to estimate the impact that TDF's patent expiration may have on the market share of Viread and the TDF/FTC combination product. In addition, examples of product extension strategies were analyzed as a way to identify and understand key issues that may allow for a successful extension strategy with GS7340.

Recent examples of exclusivity expirations demonstrate the dramatic impact generic competition can have on branded product market share. Based upon nine recent cases (Appendix A), the majority of market share loss for a branded product occurred within the first year following a generic product launch. In fact, Prozac, Glucophage and Zestril/Prinivil each lost more than 90% of its NRx market share within the first year following generic launch. Smaller products, such as Adderall, lost nearly 80% of its Nrx market share within the first year following generic launch. For Viread and the TDF/FTC combination product, we estimate significant generic competition following loss of exclusivity and estimate 80% market share loss to generics within the first year of generic competition.

In an attempt to maintain market share after generic competition, companies often develop "improved" versions of existing products and switch patients to these products before exclusivity expires. These strategies include reformulations, new NCE's, or combination products and in some cases, the new product may provide a marketing exclusivity extension. Depending upon the extension product profile, the timing of the market launch of the extension product, as well as the financial resources invested in this launch, these strategies vary in terms of their success in switching patients (Appendix B). For example, Adderall XR and Glucuphage XR were successful largely because they provided a tangible product benefit of once-daily dosing. Nexium, while undifferentiated from Prilosec, was launched with significant financial resources ($478MM spent on US advertising in 2001). On the other hand, Prozac Once-Weekly failed to switch patients largely because of its questionable efficacy, limited clinical data and short lead-time before generic competition. For GS7340 to be successful in switching patients away from TDF, GS7340 will need to be differentiated from Viread and launched well in advance of TDF's patent expiration.

Once patients are switched to a new product, market share of the new extension product can be defensible against generic competition for at least one year (Appendix C). Glucophage XR/Glucovance and Nexium were each able to defend nearly 100% of their pre-generic market share, while Adderall XR was able to double its market share in the 12 months following generic launch. Using these strategies, companies can preserve a greater percent of the original branded market share than would be possible without them. In the cases examined, the extension strategies combined with the original branded products were able to preserve on average 42% of the original market share 12 months following generic entrants (Appendix D). This decline compares favorably to the 80-90% market share decrease expected 12 months following generic competition.

Key Assumptions of the Analysis:

The following assumptions were made for purposes of calculating the potential value of GS7340 as an exclusivity extension strategy:

Exclusivity

- GS7340 maintains exclusivity through July 2021 in the US and the EU.
- Viread's exclusivity ends July 2017 in the US and EU.
- The patent for the TDF/FTC combination product does not provide exclusivity beyond 2017 in the US and the EU (the last to expire patent date of both products).

Product Profile of GS7340

- GS7340 exhibits incrementally better efficacy (greater antiviral log reduction when taken as a monotherapy) than Viread.

- The in vivo efficacy of GS7340 against virus containing the K65R mutation or thymidine analog mutations is similar to Viread.
- Th safety profile of GS7340 is comparable to TDF's safety profile.

Development

- Development of GS7340 is timed such that it is launched in 2015 with a six-year path to commercial launch.
- Two phase III registrational studies would be conducted in parallel to allow for a broad label upon approval.
- Both a single agent and a combination product (incorporating FTC) are created with GS7340; both products are launched simultaneously in 2015 based upon a parallel development path.
- Total development costs (internal and external) for GS7340 and the GS7340 combination product through product launch are estimated at $135MM and $12MM, respectively (Appendix F).

Sales and Marketing

- A 2015 commercial launch in the US and EU simultaneously; generic competition launches 2017.
- GS7340 is priced at parity to Viread: $3900/year and $3500/year in the US and EU, respectively.
- The launch of GS7340 would not expand patient market share for the tenofovir franchise, but would only cannibalize existing patients.
- Patients that are switched to the GS7340 products would not be cannibalized by the introduction of generic forms of TDF. ARV market share achieved in 2017 is maintained through 2021.
- In the first two years following generic competition, the market share of branded TDF-containing regimens will drop 80% and 90% from the pre-generic market share, respectively. In the third and following years, the 90% drop in market share is maintained.
- The decline in market share for Viread and the TDF/FTC combination product would follow a similar decline and maintain a similar long-term market share for the TDF branded products after generics are introduced, regardless if GS7340 is launched.
- A total of 96 commercial FTE's (eg. Sales, Marketing, MSL's in both the US and EU) would be devoted to commercializing GS7340 and the GS7340/FTC combination product. This represents roughly 40% of the total HIV commercial FTE's at that time.
- Yearly S&M expenses would be roughly $50MM to launch both products in the US and EU (Appendix G).
- Total US and EU ARV patients grow 3% per year with roughly 580,000 and 880,000 patients on therapy in 2003 and 2017, respectively.

- HIV treatment continues to rely upon NRTI's as the backbone of therapy.

Financial

- Discount rate of 20% given the continued risk of the program.
- The cost of goods and IOCB/Rega royalty on Net Sales of GS7340 are estimated at 13% and 2.5%, respectively.

Financial Analysis Results

Developing GS7340 as a product extension strategy for tenofovir can produce a positive net present value depending upon two main assumptions: the market share of TDF-containing regimens in 2015 and the percent of patients that can be switched from a TDF-containing to a GS7340-containing regimen before TDF's patent expiration (Table 1). As would be expected, the greater the percent ARV market share that remains on a TDF-containing regimen in 2015, the greater the NPV of developing GS7340. Estimating how successfully patients can be switched from TDF to GS7340 is difficult given GS7340's early product profile. However, one can see that for each level of TDF-market share in 2015, there is a minimum percent of patient switching required to financially justify the development of GS7340 (Table 2). In terms of ARV market share, the minimum ARV market share required to breakeven with the development of GS7340 is roughly 10%, or 85,000 patients in the US and EU. While the yearly cash flows for developing GS7340 (Appendix E) highlight the resources required to develop GS7340, the strategy can provide for a positive return if these minimum assumptions are achieved. If the product profile of GS7340 is better than our assumptions, then the pricing and development timeline assumptions may be more favorable, yielding a greater net present value.

Table 1: Net Present Value Analysis

NPV Figures in $MM's.

			ARV Patient Share on TDF-Containing Regimen at GS7340 Launch in 2015		
			30%	50%	70%
% Patients Switched to GS7340-Containing Product before Generic Competition	30%	NPV	$ (4,967)	$ 30,067	$ 65,101
		Total ARV %	*9%*	*15%*	*21%*
	45%	NPV	$ 21,309	$ 73,860	$ 126,411
		Total ARV %	*13.5%*	*22.5%*	*31.5%*
	60%	NPV	$ 47,584	$ 117,652	$ 187,721
		Total ARV %	*18%*	*30%*	*42%*

Table 2: Breakeven Analysis: Required % of Patients Switched to GS7340 for Zero NPV

	ARV Patient Share on TDF-Containing Regimen at GS7340 Launch in 2015		
	30%	50%	70%
% of TDF-Patients Switched to GS7340	33%	20%	14%

Appendix A

Market Share Impact of Generic Competition

Branded Product	Year of Generic Launch	Nrx Share of Branded Product before Generic Launch [1]	Nrx Share of Branded Product 12 Months after Generic Launch	% Drop of Brand Product Nrx Share 12 months following Generic Launch
Adderall	2002	24.9%	4.5%	**81.9%**
Augmentin	2002	37.0%	8.3%	**77.6%**
Cipro	2003	41.5%	25.1%	**39.5%** [2]
Glucophage	2002	23.8%	2.1%	**91.2%**
Prilosec	2002	13.8%	4.8%	**65.2%** [3]
Prozac	2001	12.3%	1.2%	**90.2%**
Vasotec	2000	14.0%	1.8%	**87.1%**
Zestril / Prinivil	2002	32.4%	1.7%	**94.8%**
Zovirax	1997	72.0%	28.0%	**61.1%**
		Average of Products		**83.4%** [4]

1 One month before generic launch.
2 Generic Cipro has only been available for 2 months.
3 Generic Prilosec has only been available for 8 months.
4 Average includes Zovirax, Augmentin, Adderall, Prozac, Glucophage, Vasotec, and Zestril/Prinivil.

Appendix B

Patient Switching to Extension Products before Generic Launch

Branded Product	Extension Product	Extension Product Profile	Number of Months Extension Product is Launched ahead of Generic	Branded Product NRx Share before Extension Product Launch [1]	Extension Product NRx Share at Generic Launch	% Switch from Branded to Extension Product before Generic Launch
Adderall	**Adderall XR**	*QD Dosing*	**3**	31.9%	10.1%	**31.7%**
Celexa [2]	**Lexapro**	*New NCE*	**18**	16.1% [3]	9.0%	**55.9%**
Glucophage	*Glucophage XR*	*QD Dosing*	***14***	*33.2%*	*9.0%*	*27.1%*
Glucophage	*Glucovance*	*Coformulation*	***17***	*33.2%*	*7.2%*	*21.7%*
Glucophage	**All Glucophage**					**48.8%**
Prilosec [4]	**Nexium**	*New NCE*	**21**	26.8%	15.7%	**58.6%**
Prozac	**Prozac Once-Weekly**	*Once-Weekly Dosing*	**4**	13%	0.8%	**6.2%**

1 One month before generic launch.
2 Generic versions of Celexa are not yet available, but are expected Jan 2004.
3 Represents the current sum NRx of both Celexa and Lexapro; Celexa NRx share was not at peak at Lexapro's launch.
4 Nexium has only been available for 8 months following the launch of generic Prilosec.

Appendix C

Market Share of Extension Products Following Generic Competition

Branded Product	Replacement Product	Replacement Product Nrx Share at Generic Launch	Replacement Product Nrx Share 12 months Following Generic Launch	Replacement Product % of Pre-Generic Share 12 months following Generic Launch
Adderall	Adderall XR	10.1%	22.6%	**223.8%**
Glucophage	Glucophage XR and Glucovance	16.2%	16.3%	**100.6%**
Prilosec [1]	Nexium	15.7%	17.1%	**108.9%**
Prozac	Prozac Once-Weekly	0.8%	0.6%	**75.0%**

1 Nexium has only been available for 8 months following the launch of generic Prilosec.

Appendix D

Percent Market Share Drop of Original Share with Product Extension Strategy

Branded Product	Extension Product	Original Branded NRx Share before Extension and Generic Products	Total Branded and Extension Product NRx Share 12 Months after Generic Launch	% Drop in Share of Branded and Extension Products 12 Months after Generic Competition
Adderall	Adderall XR	31.9%	27.1%	**15%**
Glucophage	Glucophage XR and Glucovance	33.2%	18.3%	**45%**
Prilosec [1]	Nexium	26.8%	20.5%	**24%**
Prozac	Prozac Once-Weekly	13.0%	2.0%	**85%**
			Average of Products	**42%**

1 Nexium has only been available for 8 months following the launch of generic Prilosec.

Appendix E

Yearly Revenue and Net Profit of GS7340

TDF ARV Marketshare of 30% in 2015

Switch 30% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$146	$242	$282	$291	$299	$308	$185
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$33	$187	$194	$216	$143

Switch 50% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$214	$355	$423	$436	$449	$463	$278
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$83	$310	$321	$346	$221

Switch 70% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$292	$485	$565	$581	$599	$617	$371
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$133	$432	$447	$476	$300

TDF ARV Marketshare of 50% in 2015

Switch 30% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$243	$404	$470	$485	$499	$514	$309
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$100	$351	$363	$389	$248

Switch 50% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$357	$592	$706	$727	$749	$771	$463
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$182	$555	$574	$606	$378

Switch 70% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$486	$808	$941	$969	$998	$1,028	$618
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$265	$760	$785	$824	$509

TDF ARV Marketshare of 70% in 2015

Switch 30% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$340	$565	$659	$678	$699	$720	$432
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$166	$514	$532	$563	$352

Switch 50% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$499	$829	$988	$1,018	$1,048	$1,080	$649
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$282	$801	$827	$867	$535

Switch 70% of Patients to GS7340

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Revenue	$0	$0	$0	$0	$0	$0	$681	$1,131	$1,317	$1,357	$1,397	$1,439	$865
Net Profit	($6)	($14)	($26)	($39)	($34)	($39)	($77)	($73)	$398	$1,088	$1,122	$1,171	$717