Potential Loss of Income

Global Sales
Billion $
Loss in Market Share

% Fall In market share

- Singulair
- Plavix
- Seroquel IR
Loss in Market Share within 4 weeks

% Fall In market share

- Singulair
- Plavix
- Seroquel IR
Modify the Drug to Keep the Patent

**ORIGIONAL DRUG**
20 Year Patent Awarded

**NEW DOSAGE**
Additional Patent Years Awarded

**NEW FORMULA**
(e.g. Child Dose)
Additional Patent Years Awarded

**HOW ‘EVERGREENING’ RESTRICTS ACCESS TO MEDICINES**

Evergreening allows pharmaceutical companies to extend monopoly protection, potentially indefinitely, by patenting modifications of an existing drug, delaying generic production of the drug beyond the original 20-year patent.

**AFFORDABLE GENERICS DELAYED**
Now you see it....
Now you don’t

Esomeprazole

S antiomer only

Slower metabolism leading to higher systemic levels in circulation
In parietal cells same effect can be achieved by doubling dose of omeprazole
Prodrug pharmacology

Tenofovir disoproxil fumarate and tenofovir alafenamide\textsuperscript{1,2}

- TAF 25mg results in >90% lower TFV plasma levels compared to TDF 300mg\textsuperscript{1,3}
- 300mg of TDF equivalent to 245mg of TD or 136mg of TFV\textsuperscript{4}

GI, gastrointestinal; OAT, organic anion transporter; TAF, tenofovir alafenamide; TD, tenofovir disoproxil; TDF, tenofovir disoproxil fumarate; TFV, tenofovir

Studies 104 & 111: E/C/F/TAF in ART-naïve adults

Plasma TFV concentrations

- 91% reduction in TFV plasma exposures with E/C/F/TAF compared with E/C/F/TDF

ART, antiretroviral therapy; C, cobicistat; E, elvitegravir; F, emtricitabine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir; SD, standard deviation

Antiviral Efficacy of TAF and TDF at Week 72

Rates of Viral Suppression
HBV DNA <29 IU/mL

- HBV DNA suppression rates were lower in HBeAg+ vs HBeAg- patients
- No significant difference between TAF and TDF
- No resistance was detected through 48 weeks

HBV DNA suppression was comparable between TAF and TDF treatment up to Week 72
Renal Laboratory Parameters in CHB Patients Treated with TAF or TDF

Study 108 and 110: Phase 3 CHB Studies: TAF vs TDF

TAF treatment had a statistically significant smaller effect on eGFR compared to TDF at 72 weeks

* p<0.001
† p<0.01

Agarwal, AASLD 2016, Poster 1844
Seto, AASLD 2016, Oral 67

Changes in BMD in CHB Patients Treated with TAF or TDF

Study 108 and 110: Phase 3 CHB Studies: TAF vs TDF

TAF treatment resulted in smaller decline in Hip and Spine BMD compared to TDF

TAF

Spine

Week 0 24 48 72
TAF, N 851 822 807 753
TDF, N 426 405 404 373

Hip

Mean (SD) % Change From Baseline, g/cm²

0 2 4

-6 -4 -2 0 2 4

Week 0 24 48 72
TAF, N 856 830 814 757
TDF, N 426 410 407 374

p-values from the ANOVA model including treatment as a fixed effect. CI, Confidence Interval

Seto, AASLD 2016, Oral 67
• Chronic kidney disease is suggested by a GFR of less than 60 ml/min/1.73m² present for at least 3 months. eGFR estimates of 90 ml/min/1.73m² or less should not be considered as evidence of kidney disease unless there is other evidence of renal damage.

• Above 89 ml/min/1.73 m² the eGFR has a wide variance (30% or more) and should not be regarded as being as accurate.
Changes in BMD in CHB Patients Treated with TAF or TDF

Study 108 and 110: Phase 3 CHB Studies: TAF vs TDF

TAF treatment resulted in smaller decline in Hip and Spine BMD compared to TDF

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<th>Week</th>
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<th>TDF, N</th>
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p-values from the ANOVA model including treatment as a fixed effect. CI, Confidence Interval

Seto, AASLD 2016, Oral 67