MODULE 2.2 – INTRODUCTION

ViiV Healthcare, in partnership with GlaxoSmithKline (GSK) is developing GSK3365791 (dolutegravir [DTG, GSK1349572] and lamivudine (3TC, GR109714) 50 mg / 300 mg fixed-dose combination (FDC, GSK3515864) tablets, for use as a complete, single tablet regimen (STR) for the treatment of HIV-1 infection in adults. As individual agents, both DTG and 3TC are currently approved products marketed as TIVICAY and EPIVIR, respectively. Based on the established tolerability and combined resistance profiles of DTG and 3TC, this simplified two-drug regimen offers favorable tolerability and suppression of resistance similar to other DTG-based HIV-1 treatment regimens. At this time, ViiV Healthcare is seeking marketing approval for the combined use of DTG and 3TC for the aforementioned indication.

Significant interest has emerged in the use of simplified, 2-drug regimens that, when compared with standard of care for 3-drug antiretroviral (ART) regimens, may reduce drug-related toxicities and potentially preserve future treatment options. The DTG + 3TC regimen currently under development and the subject of this marketing application offers a streamlined 2-drug regimen of 2 potent, well-characterized and well-tolerated ARVs. DTG + 3TC provides a novel 2-drug regimen that provides effective antiviral suppression while limiting the risk of adverse reactions associated with ARVs. The combination of 3TC with DTG, with its high barrier to resistance and ability to confer a rapid decline in HIV-1 RNA, may have a risk of selecting for resistance comparable to other 3-drug regimens.

The proposed tradename for the DTG/3TC FDC is DOVATO. To date, the DTG/3TC FDC has not received marketing approval for any indication in any market.

The Sponsor engaged the US FDA's Division of Antiviral Products (DAVP) on several occasions to discuss the DTG/3TC FDC development program. Major regulatory milestones occurred as [redacted]. [redacted] was agreed with the US FDA in [redacted], and includes [redacted]. The DAVP acknowledged its agreement with the [redacted].

The Sponsor also obtained advice from the Committee for Medicinal Products for Human Use (CHMP) regarding the [redacted] of DTG/3TC FDC in [redacted], and the [redacted] of DTG/3TC FDC in [redacted]. More recently, pre-submission meetings were held with the EMA ([redacted]), the Rapporteur (Sweden, Medical Products Agency [MPA]) in [redacted] and co-Rapporteur (Portugal, National Authority of Medicines and Health Products [INFARMED]) in [redacted]. [redacted], which includes [redacted], has been agreed with the [redacted].

To support the proposed indication for the DTG + 3TC combined regimen, the following pivotal clinical investigations of DTG and 3TC used in combination are included in this submission package:

- Phase 3 Clinical Studies 204861 (GEMINI-1) and 205543 (GEMINI-2), which demonstrated the safety of the DTG + 3TC combined regimen as well as the non-inferior antiviral activity of the DTG + 3TC combined regimen compared to compared to dolutegravir plus tenofovir/emtricitabine in HIV-1-infected treatment-naïve adults (Week 48 safety and efficacy analysis individual and pooled);
- Study 204993 (Relative Bioavailability [RBA] Study), which evaluated the relative bioavailability in the fed and fasted states of a single dose of DTG 50 mg and 3TC 300 mg as a FDC tablet compared to co-administration of a single dose of the single-entity DTG and 3TC products;
- Study 204994 (Pivotal Bioequivalence [BE] Study), which demonstrated the bioequivalence of the proposed DTG/3TC FDC to the corresponding DTG and 3TC single entities used in Phase III trials 204861 (GEMINI-1) and 205543 (GEMINI-2).

This submission also provides information regarding the nonclinical development, and includes a complete body of data for Chemistry, Manufacturing, and Controls information to support the DTG/3TC FDC tablet 50 mg / 300 mg.

In summary, the data collected in the development program suggest that the proposed DTG/3TC FDC is safe and effective for the proposed indication.