DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-977/S-011
NDA 20-977/S-012
NDA 20-978/S-013
NDA 20-978/S-014

GlaxoSmithKline
Attention: Martha Anne A. Moore, R.Ph.
Senior Director, Infectious Diseases, US Regulatory Affairs
P.O. Box 13398
Five Moore Drive
Research Triangle Park, NC 27709

Dear Ms. Moore:

We refer to your new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ziagen® (abacavir sulfate) tablets and oral solution.

April 15, 2004 Approval Letter

Fulfilled Postmarketing Commitments

We also refer to April 15, 2004 approval letter that contained the following postmarketing commitments (PMC):

PMC #1: Submit revised text to update labeling, including medication guide and Warning Card for abacavir products.

PMC #2: Study and report on available information on the management of abacavir-associated rash developing in patients who are being treated with multiple antiretroviral agents and other commonly used HIV-related drugs.

PMC #3: Submit a final report on abacavir use in adolescent patients in study PACTG 1018.

PMC #6: Submit HIV-1 viral resistance and cross-resistance data for abacavir in the Agency requested format for the agreed completed studies along with revised labeling.

PMC #7: Provide data on the *in vitro* susceptibility of NNRTI resistant HIV-1 isolates to abacavir and data on the *in vitro* susceptibility of abacavir resistant HIV-1 isolates to the FDA approved NNRTIs.

PMC #8: Conduct and submit a meta-analysis of data from abacavir clinical trials to assess the rate of psychiatric events (including depression, worsening depression, suicidal ideation/ attempt, and acute psychosis) on the abacavir versus control arms.

We have received your May 14, 2004 submission that reported on PMC 1; your June 14, 2004 submission that reported on PMC 2; your April 13, 2006 submission to IND 61,730 that reported on PMC 3; your November 16, 2004 submission that reported on PMC 6; your June 17, 2004 submission that reported on PMC 7; and your February 04, 2009 submission that reported on PMC 8.

We have reviewed the submissions listed above and conclude that PMCs 1, 2, 3, 6, 7 and 8 described in the April 15, 2004 approval letter were fulfilled.

Open Postmarketing Commitment

The following postmarketing commitment described in the April 15, 2004 approval letter is open:

PMC #4: Provide information on the status and outcome of study ACTG 321 to evaluate abacavir in neonates.

August 2, 2004 Approval Letter

Fulfilled Postmarketing Commitments

We also refer to the August 02, 2004 approval letter, which contained the following PMCs:

PMC #2: Provide human pharmacokinetic information on plasma abacavir concentrations and intracellular carbovir triphosphate [CBV-TP] concentrations following administration of abacavir 600mg once daily. Provide this information from collaborative study COL101665 following successful completion of quality assurance activity. Alternatively, if study COL101665 can not be delivered, provide this human pharmacokinetic information from a new study.

PMC #3: Assess baseline and failure RT resistance mutations and failure phenotypes of HIV-1 isolates from patients who experience virologic failure in clinical study CAL30001, a study comparing 600mg once daily abacavir versus 300mg twice daily abacavir (in combination with other drugs). Submit an analysis of genotypic and phenotypic results of study CAL30001.

PMC #5: Provide additional safety information from GSK-sponsored clinical trials utilizing abacavir plus stavudine (with other antiretroviral drugs). Specifically, provide a

report of 96-week results of study ESS40001 (an open-label, randomized study comparing the safety and efficacy of ABC/ d4T/ 3TC versus ABC/ 3TC/ EFV versus ABC/ 3TC/ 908/ RTV in therapy-naïve patients) and a summary of deaths, dropouts, and serious adverse events from other GSK-sponsored clinical studies utilizing abacavir plus stavudine.

PMC #6: Determine the in vitro combination antiretroviral activity relationships of abacavir with tenofovir, abacavir with efavirenz, and abacavir with emtricitabine.

We have received your submissions dated May 15, 2007, August 28, 2007 and October 4, 2007 that reported on PMC 2; your submission dated November 16, 2004 that reported on PMC 3;your submission dated February 28, 2005 that reported on PMC 5;and your submission dated February 10, 2005 that reported on PMC 6.

We have reviewed the submissions listed above and conclude that PMCs 2, 3, 5 and 6 described in the August 2, 2004 approval letter were fulfilled.

Open Postmarketing Commitments

The following postmarketing commitment described in the approval letter dated August 02, 2004 for efficacy supplements NDA 20-977/S012 and NDA 20-978/S014 is open:

PMC #1: Deferred pediatric study under PREA for the treatment of HIV-1 infection in pediatric patients ages 3 months to 17 years.

If you have any questions, call Rashmi Kalla, Regulatory Project Manager, at 301-796-3931.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

KENDALL A MARCUS
07/31/2009