Effect of H₂ Blockade and Food on Single-Dose Pharmacokinetics of GSK1322322, a Peptide Deformylase Inhibitor Antibacterial

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GSK1322322 is first in a new class of antibiotics, peptide deformylase inhibitors, and is active against multidrug-resistant respiratory and skin pathogens. Part 1 of this phase 1, randomized, single-dose (1,000 mg) study in 20 healthy volunteers compared the relative bioavailability of three different tablet formulations of GSK1322322 (fast release, intermediate release, and slow release) to that of the previously studied powder-in-bottle formulation to assess the optimal formulation for progression into clinical trials. Part 2 assessed the effect of a high-fat meal and drug interaction with an H₂ blocker and an H₂ blocker plus vitamin C on the pharmacokinetic profile of GSK1322322. Of the three tablet formulations, fast-release GSK1322322 provided pharmacokinetic profiles similar to those of the powder-in-bottle reference formulation (~93% relative bioavailability) and was selected for progression in part 2. When GSK1322322 was administered with a high-fat meal, the maximum observed plasma concentration ($C_{\max}$) was reduced by 20%, and the time to maximum plasma concentration ($T_{\max}$) was delayed by 1.9 h. The exposure (area under the concentration-time curve [AUC]) increased by ~20% compared to that in volunteers in the fasted state. Coadministration of GSK1322322 with an H₂ blocker resulted in a slight delay in absorption ($T_{\max}$ ~0.75 h later) and 58 and 38% decreases in the $C_{\max}$ and AUC_{0-∞} values, respectively, compared to GSK1322322 alone. This effect was reversed with vitamin C intake (i.e., no delay in $T_{\max}$ and the $C_{\max}$ and AUC_{0-∞} values decreased by only 21 and 12%, respectively). GSK1322322 was generally well tolerated, and most adverse events were mild in intensity during both parts of the study.

Resistance to antibiotics is a worldwide clinical and public health problem that continues to grow (1–3). The emergence of antibiotic-resistant infections for which there are limited treatment options represents a critical unmet medical need. GSK1322322 is a potent inhibitor of peptide deformylase (PDF); PDF inhibitors are a new class of antibiotics (4). A clinically unexploited target, PDF is an essential bacterial enzyme required for protein maturation (5, 6). GSK1322322 is a member of a novel hydrazinopyrimidine class of PDF inhibitors discovered through a combination of structure-based drug design and iterative medicinal chemistry (7). GSK1322322 shows no target-based cross-resistance with currently used agents (8).

GSK1322322 is active against multidrug-resistant respiratory and skin pathogens, including multidrug-resistant *Streptococcus pneumoniae* and methicillin-resistant *Staphylococcus aureus* (4, 8, 9). *In vitro*, GSK1322322 exhibits a potent sub-MIC effect for most strains of *S. aureus*, inhibiting growth for 6 to 8 h at concentrations of $\leq 1/8$ the MIC (10, 11). In addition, potent *in vivo* activity of GSK1322322 against rodent respiratory tract infection and skin and soft tissue infection models has also been demonstrated (4, 8).

In a single-dose pharmacokinetic (PK), first-time-in-human phase 1 study in healthy volunteers, GSK1322322 was administered as a powder-in-bottle formulation that demonstrated a favorable PK profile (9). In part 1 of this two-part, single-dose study, the relative bioavailability of three tablet formulations was compared to that of the powder-in-bottle formulation to determine which formulation to use in future studies. The investigational GSK1322322 tablet formulation selected for progression was further evaluated in part 2 of the study to understand the effect of food on the solubility and absorption of the drug in this formulation. In the first-time-in-human study, the administration of GSK1322322 as the powder-in-bottle formulation with a high-fat

meal reduced the rate of absorption without affecting the extent of absorption. In addition, because the solubility of GSK1322322 was shown to decrease with increasing pH (>50 mg/ml at pH 3.5 and <1 mg/ml at pH 7) in an *in vitro* study, the selected GSK1322322 tablet formulation was evaluated for the effect of coadministration of an H₂ blocker alone or an H₂ blocker given in combination with vitamin C (ascorbic acid) on GSK1322322 single-dose PK.

MATERIALS AND METHODS

Study design and population. This was a randomized, open-label, single-dose, balanced-crossover, two-part study of healthy volunteers (study identifier PDF112034). Adults aged 18 to 65 years, who were in generally good health with no clinically relevant abnormalities, as determined by medical history, physical examination, laboratory tests, and cardiac monitoring, were eligible for the trial. The volunteers needed a body mass index of 18.5 to 29.9 kg/m², inclusive. All volunteers had a QT duration corrected (QTc) for heart rate using Bazett's formula of <450 ms (or a QTc of <480 ms in volunteers with bundle branch block). Volunteers were excluded from the study if they demonstrated one of the following conditions: a positive prestudy drug/alcohol screen test result; a positive hepatitis B surface antigen or hepatitis C antibody result within 3 months of screening; a chronic history of or current liver disease; a positive test result for HIV antibody; use of any investigational drug within 30 days, 5 half-lives, or twice the duration of the biological effect of the investiga-

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tional drug (whichever is longer) before the day of dosing; or exposure to more than four new chemical entities within 12 months before the day of dosing. All volunteers provided written informed consent. The study was approved by IntegReview Ethical Review Board (Austin, TX) and was conducted in accordance with good clinical practice at the Buffalo Clinical Research Center, LLC (Buffalo, NY).

Part 1 of the trial was planned with a four-period crossover design to assess the single-dose (1,000 mg) safety and relative bioavailability of three different GSK1322322 tablet formulations (treatment A, fast release; treatment B, intermediate release; and treatment C, slow release) compared to a powder-in-bottle (treatment R, reference) formulation. These formulations were administered after an overnight fast of ≥ 10 h. The volunteers were admitted to the clinical unit on day 1 and remained in the unit until day 12. Each volunteer received a total of four single doses of 1,000 mg of GSK1322322 in an open-label, randomized fashion with a washout period of ≥ 3 days between doses. In part 2 of the study, the optimal formulation based on the PK results from part 1 of the study (i.e., the fast-release tablet formulation) was used to estimate the effect of a high-fat meal (treatment OF), a histamine 2 (H_2) blocker alone (treatment OH), or an H_2 blocker plus vitamin C (treatment OC) on the PK of GSK1322322 following a single dose (1,000 mg) of the formulation. The same volunteers who took part in part 1 of the study also participated in part 2 of the study. In part 2, they were admitted to the clinical unit on day 1 and remained in the unit until day 9. Each volunteer received a total of three single 1,000-mg doses of GSK1322322 with either a high-fat meal, an H_2 blocker alone, or an H_2 blocker in combination with vitamin C in an open-label, randomized fashion with a washout period of ≥ 3 days between doses. For treatment OF, volunteers took the study medication with a standard high-fat meal (53% of calories from fat), which included two slices of toasted white bread with two teaspoons of butter, two eggs fried in butter, two slices of bacon, 4 oz. of hash-browned potatoes, and 8 oz. of whole milk (32.1 g of protein, 70.2 g of carbohydrate, and 51.1 g of fat). For treatments OH and OC, two doses of H_2 blocker (150 mg of ranitidine) were administered on the evening before and the morning of GSK1322322 intake (≥ 90 min before dosing). In addition, for treatment OC, 1,000 mg of vitamin C was administered 5 min before GSK1322322 intake.

Each volunteer participated in the present study for approximately 12 to 13 weeks, which included a 30-day screening period, a 3-week treatment period in parts 1 and 2, and a follow-up period of 7 to 10 days. There was a washout period of 3 to 4 weeks between parts 1 and 2 of the study, during which time the PK samples from part 1 were analyzed, and the optimal tablet formulation for assessment in part 2 of the study was selected.

Pharmacokinetic assessments. Blood samples for the measurement of plasma GSK1322322 concentrations were collected before (within 15 min before dosing) and for a 48-h period (i.e., at 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, 18, 24, 36, and 48 h) after GSK1322322 administration. Plasma GSK1322322 concentrations were determined by Worldwide Bioanalysis (GlaxoSmithKline, King of Prussia, PA) using high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS). Briefly, GSK1322322 was extracted from the plasma samples using acetonitrile containing [$^{13}C_2$, $^{15}N_2$]GSK1322322 as an internal standard. Extracts were then analyzed by HPLC-MS/MS using a TurbolonSpray interface with positive-ion multiple reaction monitoring (AB Sciex, Framingham, MA). Plasma concentrations of GSK1322322 were determined by using a standard calibration curve constructed with standard solutions prepared with human plasma. Using a 25- μ l aliquot of plasma, the lower limit of quantification for the assay was 5.0 ng/ml, and the upper limit of quantification was 5,000 ng/ml. The calibration curve was linear over this range. Each batch of plasma samples was run against duplicate freshly prepared calibration standards. Quality control samples at three concentrations (20, 150, and 4,000 ng/ml) were also included in the run. PK analyses of plasma GSK1322322 concentration-time data were conducted using the noncompartmental model 200 (for extravascular admin-

TABLE 1 Volunteer demographics

Characteristic	Data for all volunteers (n = 20) ^a
Mean age (yr)	29.2 (10.7)
No. (%) of male volunteers	20 (100)
Mean BMI ^b (kg/m ²)	25.7 (2.8)
Mean ht (cm)	176.5 (8.0)
Mean wt (kg)	80.5 (12.7)
Ethnicity, no. of volunteers (%)	
Hispanic or Latino	1 (5)
Not Hispanic or Latino	19 (95)
Race, no. of volunteers (%)	
African American/African heritage	11 (55)
White/Caucasian/European heritage	9 (45)

^a Each value is expressed as indicated in column 1. Unless specified otherwise in column 1, the value in parentheses is the standard deviation.

^b BMI, body mass index.

istration) of WinNonlin, version 5.2 (Pharsight Corp., Mountain View, CA). The plasma PK parameters assessed included the area under the plasma concentration-time curve (AUC), the maximum observed plasma concentration (C_{max}), the time to maximum plasma concentration (T_{max}), and the terminal elimination half-life ($t_{1/2}$).

Safety assessments. Safety was assessed by evaluating reported and observed adverse events (AEs), reviewing electrocardiograms (ECGs), measuring vital signs, Holter monitoring, and conducting physical examinations and clinical laboratory tests (i.e., chemistry, hematology, and urinalysis). Twelve-lead ECGs were obtained at screening, at day -1, and predose on days 1, 4, 7, and 10 (part 1 only).

Statistical analyses. Baseline and demographic characteristics, safety data, and PK parameters were summarized using descriptive statistics. Statistical analyses were performed using SAS software (version 9.1; SAS Institute, Cary, NC). An estimation approach was undertaken in order to estimate the effect of food, as well as the effect of an H_2 blocker on the PK of GSK1322322. All PK parameters, except T_{max} , were $\log_e$ transformed. The effect of food was estimated as the ratio of geometric least-squares means of the fed treatment (treatment OF) to that of the reference (fasted) treatment A, with corresponding 90% confidence intervals (CIs). The fasted treatment for the selected optimal tablet formulation from part 1 (treatment A) was considered the reference treatment. Similarly, the effect of an H_2 blocker alone and of an H_2 blocker in combination with vitamin C was estimated as the ratio of geometric least-squares means for the test treatments (treatments OH and OC) to that of the reference treatment identified from part 1 (treatment A), with corresponding 90% CI values. The T_{max} of GSK1322322 was analyzed nonparametrically using the Wilcoxon method. The point estimates and 90% CI values for the median differences were computed.

RESULTS

Of the 20 volunteers enrolled in the study, all completed part 1 and 16 completed part 2 of the study. Four volunteers withdrew from the study for the following reasons: one because of a scheduling issue after completing part 1, one because of a family emergency on day 3 of part 2, one at the investigator's discretion because of an elevated alanine aminotransferase concentration (73 IU/liter) on day -1 of part 2, and one because of a serious AE (multiple gunshot wounds) between parts 1 and 2 of the study. Overall, the volunteers enrolled in this study had a mean age of 29 years, and all were male (Table 1).

Pharmacokinetics. In part 1 of the study, following single-dose oral administration in 3 different tablet formulations and a powder-in-bottle formulation, GSK1322322 was absorbed rap-

TABLE 2 Plasma PK parameters for three GSK1322322 tablet formulations and a powder-in-bottle formulation

Parameter	Mean value (CVb [%]) ^a			
	Treatment A, fast release (n = 20)	Treatment B, intermediate release (n = 20)	Treatment C, slow release (n = 20)	Treatment R, powder in bottle (n = 20)
AUC _{0-t} (μg·h/ml)	25.4 (36)	19.6 (42)	14.9 (43)	27.0 (32)
AUC _{0-∞} (μg·h/ml)	25.6 (35)	19.6 (43)*	15.0 (42)	27.2 (31)
C _{max} (μg/ml)	8.82 (54)	4.29 (55)	3.53 (52)	9.41 (63)
t _{1/2} (h)	8.1 (44)	6.4 (25)*	7.0 (31)	8.5 (49)
T _{max} (h) ^b	0.50 (0.3–2.5)	1.5 (0.5–6.0)	1.0 (0.5–2.5)	0.75 (0.2–2.5)

^a CVb, between-volunteer coefficient of variation. *, n = 19. Data are as defined in column 1, except as noted for T_{max}.
^b T_{max} values are presented as the median (range) for each treatment.

idly, with median T_{max} values ranging from 0.5 to 1.5 h (Table 2). GSK1322322 was eliminated, with mean t_{1/2} values ranging from 6.4 to 8.5 h. Moderate to high intervolunteer variability was observed with C_{max} (between-volunteer coefficient of variation [CVb] range, 52 to 63%) and AUC (CVb ranges, 32 to 43% for AUC_{0-t} [i.e., the AUC from time zero to the last quantifiable time point] and 31 to 43% for AUC_{0-∞}) estimates for these formulations. Of the three tablet formulations, the fast-release GSK1322322 formulation provided PK profiles similar to those of the powder-in-bottle reference formulation. Administration of the fast-release GSK1322322 formulation resulted in ~93% relative bioavailability compared to the powder-in-bottle formulation, based on both AUC_{0-∞} and C_{max} data (Table 3). However, the relative bioavailabilities of the intermediate-release and slow-release formulations were 69 and 55% compared to the powder-in-bottle formulation, respectively, based on the AUC_{0-∞} data. Therefore, the fast-release formulation was considered an optimal tablet formulation and was used in part 2 of this study.

In part 2 of our study, when the GSK1322322 tablet formulation was administered with a high-fat meal, C_{max} was reduced by 20% (7.1 μg/ml versus 8.8 μg/ml), T_{max} was delayed by 1.9 h (2.5 versus 0.5 h), and AUC increased by ~20% (AUC_{0-t} of 30.4 μg·h/ml versus 25.4 μg·h/ml and AUC_{0-∞} of 30.8 μg·h/ml versus 25.6 μg·h/ml) compared to volunteers in the fasted state (treat-

TABLE 3 Statistical assessment of GSK1322322 PK parameters of comparators versus GSK1322322 powder-in-bottle reference formulation (treatment R)^a

Parameter	Treatment comparison			
	Point estimate ^b	90% CI	CVw (%)	
AUC _{0-∞}	A vs R	0.93	0.79–1.10	31.3
	B vs R	0.69	0.59–0.82	31.3
	C vs R	0.55	0.47–0.65	31.3
C _{max}	A vs R	0.93	0.73–1.18	46.5
	B vs R	0.45	0.36–0.57	46.5
	C vs R	0.38	0.30–0.48	46.5

^a Treatment A, fast-release GSK1322322 tablet formulation; treatment B, intermediate-release GSK1322322 tablet formulation; treatment C, slow-release GSK1322322 tablet formulation; CVw, weighted coefficient of variation.
^b That is, the ratio of the geometric means.

TABLE 4 Plasma PK parameters for three treatments with the fast-release tablet formulation

Parameter	Mean value (CVb [%]) ^a for various fast-release GSK1322322 tablet formulations			
	Treatment A (n = 20)	Treatment OF (n = 17)	Treatment OH (n = 17)	Treatment OC (n = 16)
AUC _{0-t} (μg·h/ml)	25.4 (36)	30.4 (20)	15.9 (41)	22.7 (26)
AUC _{0-∞} (μg·h/ml)	25.6 (35)	30.8 (20)*	16.0 (40)	22.9 (26)
C _{max} (μg/ml)	8.82 (54)	7.12 (24)	3.72 (38)	7.04 (42)
t _{1/2} (h)	8.1 (44)	8.0 (23)*	7.6 (40)	7.1 (45)
T _{max} (h) ^b	0.50 (0.3–2.5)	2.5 (1.5–6.0)	1.0 (0.5–3.0)	0.5 (0.3–2.0)

^a CVb, between-volunteer coefficient of variation; treatment OC, fast-release GSK1322322 tablet formulation with an H₂ blocker and vitamin C; treatment OF, fast-release GSK1322322 tablet formulation with a high-fat meal; treatment OH, fast-release GSK1322322 tablet formulation with an H₂ blocker. Data for treatment A reflect the PK data for the fast-release tablets from part 1 of the study. Data are as defined in column 1, except as noted for T_{max}. *, n = 16.
^b T_{max} values are presented as the median (range) for each treatment.

ment A of part 1; Tables 4 and 5, Figure 1). Although food lowered the rate of absorption, it did not substantially affect the extent of GSK1322322 absorption. The between-volunteer variability in PK parameters was smaller when the tablet was administered with food (CVb ranged up to 20 and 24% for AUC_{0-t} and C_{max}, respectively, with food, compared to up to 36 and 54% for AUC_{0-t} and C_{max}, respectively, when tablets were administered in the fasted state).

TABLE 5 Statistical assessment of GSK1322322 PK parameters of comparators versus GSK1322322 alone

Parameter	Fast-release tablet formulation ^a			
	Treatment comparison	Point estimate ^b	90% CI	CVw (%)
AUC _{0-t}	OC vs A	0.88	0.75–1.04	30.3
	OF vs A	1.19	1.01–1.40	30.3
	OH vs A	0.62	0.53–0.73	30.3
AUC _{0-∞}	OC vs A	0.88	0.74–1.04	30.5
	OF vs A	1.19	1.01–1.41	30.5
	OH vs A	0.62	0.53–0.73	30.5
C _{max}	OC vs A	0.79	0.64–0.98	39.2
	OF vs A	0.80	0.65–0.99	39.2
	OH vs A	0.42	0.34–0.52	39.2
t _{1/2}	OC vs A	0.90	0.75–1.07	31.4
	OF vs A	0.99	0.84–1.18	31.4
	OH vs A	0.95	0.80–1.13	31.4
T _{max}	OC vs A	0	–0.25–0.13	
	OF vs A	1.88	1.25–2.50	
	OH vs A	0.75	0.13–1.25	

^a Treatment A, fast-release GSK1322322 tablet formulation in part 1 of the study; CVw, weighted coefficient of variation; treatment OC, fast-release GSK1322322 tablet formulation with an H₂ blocker and vitamin C; treatment OF, fast-release GSK1322322 tablet formulation with a high-fat meal; treatment OH, fast-release GSK1322322 tablet formulation with an H₂ blocker.
^b That is, the ratio of the geometric means for AUC, C_{max}, and t_{1/2} values and the median difference for T_{max}.

FIG 1 Mean plasma concentration of GSK1322322 over time, by regimen. Regimen A, fast-release GSK1322322 tablet formulation; regimen OC, fast-release GSK1322322 tablet formulation with an H_2 blocker and vitamin C; regimen OF, fast-release GSK1322322 tablet formulation with a high-fat meal; regimen OH, fast-release GSK1322322 tablet formulation with an H_2 blocker.

Relative to the GSK1322322 tablet formulation alone (treatment A of part 1), coadministration of GSK1322322 tablet formulation with an H_2 blocker resulted in a slight delay in absorption ($T_{max} \sim 0.75$ h later) and a decrease in the C_{max} (58%), AUC_{0-t} (38%), and $AUC_{0-\infty}$ (38%) values. Coadministration of GSK1322322 tablet formulation with an H_2 blocker and vitamin C showed that vitamin C can somewhat overcome the reduced bioavailability of GSK1322322 observed with the administration of the H_2 blocker alone. There was no delay in absorption, and $AUC_{0-\infty}$ and C_{max} were decreased by only 12 and 21%, respectively.

Safety. GSK1322322 was well tolerated when administered as three tablet formulations in part 1 of the study and when coadministered with food, an H_2 blocker alone, or the combination of an H_2 blocker and vitamin C in part 2 of the study (Table 6). There were few AEs or drug-related AEs during the study. The most frequently reported AEs in the study (in both parts 1 and 2) included flatulence ($n = 3$) and headache ($n = 3$). All other AEs were reported in only one volunteer each. All AEs were mild in inten-

sity, except for a serious AE (gunshot wounds) in 1 volunteer, which was severe in intensity. This event was not related to the study drug and occurred during the 3-week washout period between part 1 and part 2 of the study. The most commonly reported drug-related AE was flatulence ($n = 2$). No significant trends or changes from baseline in vital signs, ECGs, or clinical laboratory parameters were observed.

DISCUSSION

In the first part of this two-part phase 1 study, three different tablet formulations of GSK1322322 (fast release, intermediate release, and slow release) were assessed to select a tablet formulation for use in future clinical studies. Prior to this study, GSK1322322 was evaluated only as a powder-in-bottle formulation (9). Of the three tablet formulations evaluated, the fast-release formulation provided a PK profile similar to that of the powder-in-bottle reference formulation, with 93% relative bioavailability, and was selected for progression to part 2 of the study.

In part 2 of the study, administration of the GSK1322322 tablet

TABLE 6 Summary of adverse events

Adverse event	No. of events (%) ^a						
	Part 1				Part 2		
	Treatment A (n = 20)	Treatment B (n = 20)	Treatment C (n = 20)	Treatment R (n = 20)	Treatment OF (n = 17)	Treatment OH (n = 17)	Treatment OC (n = 16)
All adverse events	2 (10)	3 (15)	1 (5)	0	4 (24)	0	1 (6)
Flatulence	2 (10)	0	0	0	1 (6)	0	0
Headache	0	0	1 (5)	0	1 (6)	0	1 (6)
Abdominal pain, upper	0	0	0	0	1 (6)	0	0
Application site irritation	0	1 (5)	0	0	0	0	0
Infusion site erythema	0	1 (5)	0	0	0	0	0
Dizziness	0	0	0	0	0	0	1 (6)
Palpitations	0	0	0	0	1 (6)	0	0
Gunshot wound	0	1 (5)	0	0	0	0	0

^a Treatment A, fast-release GSK1322322 tablet formulation; treatment B, intermediate-release GSK1322322 tablet formulation; treatment C, slow-release GSK1322322 tablet formulation; treatment OC, fast-release GSK1322322 tablet formulation with an H₂ blocker and vitamin C; treatment OF, fast-release GSK1322322 tablet formulation with a high-fat meal; treatment OH, fast-release GSK1322322 tablet formulation with an H₂ blocker; treatment R, powder-in-bottle GSK1322322 formulation.

formulation with the high-fat meal lowered the rate of GSK1322322 absorption but did not affect the extent of absorption (AUC). The finding from this current intravolunteer comparison is similar to what was observed with the powder-in-bottle formulation in a single-dose first-time-in-human study (intervolunteer comparison) (9). Because the primary driver for efficacy is AUC (12), the 20% decrease in $C_{\max}$ with the concomitant 20% increase in AUC is not considered clinically significant.

In an *in vitro* study, the solubility of GSK1322322 was shown to decrease with increasing pH. The effect of H₂ blocker coadministration on the GSK1322322 PK profile was evaluated here to test the effect of increasing gastric pH. Coadministration of an H₂ blocker with GSK1322322 resulted in a slight delay in absorption (5%) and decreases in $C_{\max}$ (58%) and AUC_{0-∞} (38%). To evaluate the ability of vitamin C to reduce or reverse the H₂ blocker effect on the absorption of GSK1322322, 1,000 mg of vitamin C was coadministered in these volunteers. It is believed that coadministration of vitamin C can reduce gastric pH changes induced by an H₂ blocker. Intake of vitamin C nearly reversed the effect of an H₂ blocker.

In all arms of the second phase of this study, a second peak was observed ~4 h after receiving the fast-release GSK1322322 tablet alone, in combination with an H₂ blocker, or in combination with vitamin C. This second peak is likely the result of enterohepatic circulation of GSK1322322, which is known to undergo hepatic metabolism to an N-glucuronide in humans (unpublished data), which is likely unstable and readily undergoes degradation to GSK1322322 in the gut before being reabsorbed.

GSK1322322 was well tolerated in both parts of the study. All AEs were mild in intensity, except for a serious AE (gunshot wounds) that was not related to the study drug. Because of its favorable PK characteristics and safety profile, GSK1322322 has the potential to be a first-in-class PDF inhibitor for clinical use. The favorable PK profile of the fast-release GSK1322322 tablet formulation supports progression of this formulation in future studies.

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