Table 3. Pharmacokinetic Parameters Following More Than One Dose of DS102.

Pharmacokinetic Parameters	100 mg Fasted (N=0)	500 mg Fasted (N=2)	1000 mg Fasted (N=3)	2000 mg Fasted (N=3)
AUC0-24 (ng•hr/mL)[a]	.	.	.	.
AUC0-last (ng•hr/mL)[a]	.	1270 (70.9)	1063 (102.6)	733.3 (56.5)
AUC0-inf (ng•hr/mL)[a]	.	.	.	.
AUC%extrap (ng•hr/mL)[a]	.	.	.	.
Cmax (ng/mL)[a]	.	343.7 (52.1)	366.2 (102.5)	294.3 (70.1)
Tmax (hr)[c]	.	6.005 (6.00, 6.01)	5.996 (5.99, 6.00)	8.001 (8.01, 8.01)
Tlast (hr)[c]	.	8.001 (8.00, 8.00)	7.999 (8.00, 8.00)	8.001 (8.00, 8.01)
Kel (1/hr)[b]	.	.	.	.
t1/2 (hr)[b]	.	.	.	.

100 mg DS102 fasted on Day 1
500 mg DS102 fasted on Day 1
1000 mg DS102 fasted on Day 1
2000 mg DS102 fasted on Day 1

[a]: Presented as geom. mean (geom. CV%)
[b]: Presented as mean ± SD
[c]: Presented as median (minimum, maximum)
.: Not reportable.

PK parameters were not calculable for any subject following 100 mg Fasted.
PK parameters were not calculable for Subjects 9, 12, 15, and 16 following 500 mg Fasted.
PK parameters were not calculable for Subjects 20, 23, and 24 following 1000 mg Fasted.
PK parameters were not calculable for Subjects 29, 31, and 32 following 2000 mg Fasted.

[0068] As shown in Table 3, the median Tmax values were 6.00 hours for both the 500 mg and 1000 mg dose levels and 8.00 hours for the 2000 mg dose level. For all 3 cohorts in the fasted state, PK parameters were only calculated for the 2 or 3 subjects with sufficient data. Exposure parameters (Cmax and AUC0-last) were highly variable and should be interpreted with caution, with geometric mean coefficient of variation (CV%) above 50%.

Table 4. Pharmacokinetic Parameters Following a Single Dose of DS102.

[0069] As shown in Table 4, the median Tmax values following single-dose administration of 500 mg DS102 after a standard and high-fat diet were 4.00 hours and 6.00 hours, respectively. For both treatment regimens, PK parameters were calculated for the 6 subjects who received DS102, except for AUC0-inf and t½ which were calculable for only 4 subjects following a standard diet.

Pharmacokinetic Parameters	500 mg Fasted (N=2)	500 mg Fed Standard Diet (N=6)	500 mg Fed High Fat Diet (N=6)
AUC0-24 (ng*hr/mL)[a]	.	18840(17.9)	.
AUC0-last (ng*hr/mL)[a]	1270(70.9)	8450(67.7)	9693(51.9)
AUC0-inf (ng*hr/mL)[a]	.	11050(19.7)	.
AUC%extrap (ng*hr/mL)[a]	.	7.543e+9.7728	.
Cmax (ng/mL)[b]	343.7(32.1)	2420(62.1)	2402(64.7)
Tmax (hr)[c]	6.995(6.00, 6.01)	4.014(2.00, 8.01)	6.021(4.00, 7.99)
Tlast (hr)[c]	8.001(8.00, 8.00)	8.017(8.00, 12.00)	11.995(8.00, 12.01)
Kel (1/hr)[a]	.	0.4711+-0.22228	.
T1/2 (hr)[a]	.	1.998+-1.3155	.

500 mg DS102 fasted on Day 1
500 mg DS102 fed- standard diet on Day 1
500 mg DS102 fed- high fat diet on Day 1

a
[illegible]
b. Presented as mean+-SD
c
[illegible]
.: Not reportable.

PK parameters were not calculable for Subjects 9, 12, 13 and 16 following 500 mg Fasted

[0070] As shown in Tabe 5, following a standard diet, the mean 15(S)-HEPE t½ was 2.00 hours. No clear elimination phase was apparent following a high-fat diet. Though data were highly variable, it was apparent that a standard or high-fat diet increased mean maximum and overall exposure of 15(S)-HEPE (based on Cmax and AUC0-last, respectively) relative to the fasted condition. Moreover, 15(S)-HEPE exposure following a single oral dose of 500 mg DS102 appeared higher under fed conditions relative to higher doses (1000 mg and 2000 mg) under fasted conditions. Compared to when DS102 was given with a standard diet, the apparition of 15(S)-HEPE in plasma given with a high-fat diet was delayed by 2 hours. Due to the high variability, it was not possible to determine if the extent of exposure was different following a high-fat versus standard diet using noncompartmental methods.

Table 5. Pharmacokinetic Parameters at Days 1, 14, and 28.

	500 mg QD - Fasted		
Pharmacokinetic Parameters	Day 1 (N=6)*	Day 14 (N=3)	Day 28 (N=2)
AUC0-24 (ng*hr/mL)[a]	6240	.	.
AUC0-last (ng*hr/mL)[a]	1681 (156.6)	2370 (106.8)	2787 (92.6)
AUC0-inf (ng*hr/mL)[a]	6277	.	.
AUC%extrap (ng*hr/mL)[a]	9.411	.	.
Cmax (ng/mL)[a]	459.1 (119.5)	644.1 (68.3)	737.4 (67.9)
Tmax (hr)[b]	5.065 (4.00, 8.14)	5.895 (3.98, 6.01)	6.004 (6.00, 6.01)
Tlast (hr)[b]	8.079 (8.00, 12.00)	8.034 (8.00, 12.00)	10.002 (8.01, 12.00)
Kel (1/hr)[a]	0.2455	.	.
t1/2 (hr)[a]	2.824	.	.
RAUC[c]	.	6.807 ± 10.322	8.205 ± 10.210
RCmax[c]	.	4.177 ± 3.4055	5.923 ± 6.8329

500 mg DS102 QD fasted on Days 1 - 28

a. [illegible]
b. Presented as mean ± SD
c. [illegible]
.: Not reportable.

*AUC0-24, AUC0-inf, AUC%extrap, Kel, and t½ were reported only for Subject 38.
PK parameters were not calculable for Subjects 34, 37, and 39 on Day 14.
PK parameters were not calculable for Subjects 34, 37, 39, and 136 on Day 28.

[0071] *Safety Results.* There were no deaths, serious adverse events (SAEs), or subject discontinuations due to AEs reported in this study. No trend was observed in single or multiple ascending doses of DS102 with regard to subject incidence for AE reporting and was comparable to AE reporting following placebo. The PI considered the majority of events to be mild in intensity and not related to the study treatment. The majority of the events reported were considered not related to the study treatment with events of dysguesia and eructation (following DS102 treatment) considered related. There were several laboratory events reported as AEs during the study in Parts 1 and 2. All laboratory reported events were mild in intensity and considered not related to the study treatment.

[0072] Single ascending doses of 100 mg, 500 mg, 1000 mg and 2000 mg DS102 and multiple ascending doses of 500 mg, 500 and 1000 mg were safe and well tolerated in the healthy subjects in this study.

[0073] PK profiles of 15(S)-HEPE in healthy subjects following single oral administration of 100 mg, 500 mg, 1000 mg, or 2000 mg DS102 and following multiple

Table 3. Pharmacokinetic Parameters Following More Than One Dose of DS102.

Pharmacokinetic Parameters	100 mg Fasted (N=0)	500 mg Fasted (N=2)	1000 mg Fasted (N=3)	2000 mg Fasted (N=3)
AUC0-24 (ng•hr/mL)[a]	.	.	.	.
AUC0-last (ng•hr/mL)[a]	.	1270 (70.9)	1063 (102.6)	733.3 (56.5)
AUC0-inf (ng•hr/mL)[a]	.	.	.	.
AUC%extrap (ng•hr/mL)[b]	.	.	.	.
Cmax (ng/mL)[a]	.	343.7 (52.1)	366.2 (102.5)	294.3 (70.1)
Tmax (hr)[c]	.	6.005 (6.00, 6.01)	5.996 (5.99, 6.00)	8.001 (6.01, 8.01)
Tlast (hr)[c]	.	8.001 (8.00, 8.00)	7.999 (8.00, 8.00)	8.001 (8.00, 8.01)
Kel (1/hr)[b]	.	.	.	.
t1/2 (hr)[b]	.	.	.	.

100 mg DS102 fasted on Day 1
500 mg DS102 fasted on Day 1
1000 mg DS102 fasted on Day 1
2000 mg DS102 fasted on Day 1

[a]: Presented as geom. mean (geom. CV%)
[b]: Presented as mean ± SD
[c]: Presented as median (minimum, maximum)
.: Not reportable.

PK parameters were not calculable for any subject following 100 mg Fasted.
PK parameters were not calculable for Subjects 9, 12, 15, and 16 following 500 mg Fasted.
PK parameters were not calculable for Subjects 20, 23, and 24 following 1000 mg Fasted.
PK parameters were not calculable for Subjects 29, 31, and 32 following 2000 mg Fasted.

[0068] As shown in Table 3, the median Tmax values were 6.00 hours for both the 500 mg and 1000 mg dose levels and 8.00 hours for the 2000 mg dose level. For all 3 cohorts in the fasted state, PK parameters were only calculated for the 2 or 3 subjects with sufficient data. Exposure parameters (Cmax and AUC0-last) were highly variable and should be interpreted with caution, with geometric mean coefficient of variation (CV%) above 50%.

Table 4. Pharmacokinetic Parameters Following a Single Dose of DS102.

[0069] As showin in Table 4, the median Tmax values following single-dose administration of 500 mg DS102 after a standard and high-fat diet were 4.00 hours and 6.00 hours, respectively. For both treatment regimens, PK parameters were calculated for the 6 subjects who received DS102, except for AUC0-inf and t½ which were calculable for only 4 subjects following a standard diet.

Pharmacokinetic Parameters	500 mg Fasted (N=2)	500 mg Fed Standard Diet (N=6)	500 mg Fed High Fat Diet (N=6)
AUC0-24 (ng*hr/mL)[a]	.	10940 (17.9)	.
AUC0-last (ng*hr/mL)[a]	1270 (70.9)	8450 (67.7)	9693 (51.9)
AUC0-inf (ng*hr/mL)[a]	.	11050 (19.7)	.
AUC%extrap (ng*hr/mL)[b]	.	7.543 ± 9.7728	.
Cmax (ng/mL)[a]	343.7 (52.1)	2420 (62.1)	2402 (64.7)
Tmax (hr)[c]	6.005 (6.00, 6.01)	4.014 (2.00, 6.01)	6.021 (4.00, 7.99)
Tlast (hr)[c]	8.001 (8.00, 8.00)	8.017 (8.00, 12.00)	11.993 (8.00, 12.01)
Kel (1/hr)[b]	.	0.4711 ± 0.22828	.
t1/2 (hr)[b]	.	1.998 ± 1.5155	.

500 mg DS102 fasted on Day 1
500 mg DS102 fed - standard diet on Day 1
500 mg DS102 fed - high fat diet on Day 1

a. Presented as geom. mean (geom. CV%)
b. Presented as mean ± SD
c. Presented as median (minimum, maximum)
.: Not reportable.

PK parameters were not calculable for Subjects 9, 12, 15 and 16 following 500 mg Fasted.

[0070] As shown in Tabe 5, following a standard diet, the mean 15(S)-HEPE t½ was 2.00 hours. No clear elimination phase was apparent following a high-fat diet. Though data were highly variable, it was apparent that a standard or high-fat diet increased mean maximum and overall exposure of 15(S)-HEPE (based on Cmax and AUC0-last, respectively) relative to the fasted condition. Moreover, 15(S)-HEPE exposure following a single oral dose of 500 mg DS102 appeared higher under fed conditions relative to higher doses (1000 mg and 2000 mg) under fasted conditions. Compared to when DS102 was given with a standard diet, the apparition of 15(S)-HEPE in plasma given with a high-fat diet was delayed by 2 hours. Due to the high variability, it was not possible to determine if the extent of exposure was different following a high-fat versus standard diet using noncompartmental methods.

Table 5. Pharmacokinetic Parameters at Days 1, 14, and 28.

	500 mg QD - Fasted		
Pharmacokinetic Parameters	**Day 1 (N=6)***	**Day 14 (N=3)**	**Day 28 (N=2)**
AUC0-24 (ng*hr/mL)[a]	6249	.	.
AUC0-last (ng*hr/mL)[a]	1681 (156.6)	2370 (106.8)	2787 (92.6)
AUC0-inf (ng*hr/mL)[a]	6277	.	.
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Cmax (ng/mL)[a]	459.1 (119.5)	644.1 (68.3)	737.4 (67.9)
Tmax (hr)[c]	5.005 (4.00, 8.14)	5.995 (5.99, 6.01)	6.004 (6.00, 6.01)
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Kel (1/hr)[b]	0.2455	.	.
t1/2 (hr)[b]	2.824	.	.
RAUC[b]	.	6.807 ± 10.322	8.205 ± 10.210
RCmax[b]	.	4.177 ± 5.4055	5.923 ± 6.8329

500 mg DS102 QD fasted on Days 1 - 28

[a]: Presented as geom mean (geom CV%)
[b]: Presented as mean ± SD
[c]: Presented as median (minimum, maximum)
.: Not reportable.

*AUC0-24, AUC0-inf, AUC%extrap, Kel, and t½ were reported only for Subject 38.
PK parameters were not calculable for Subjects 34, 37, and 39 on Day 14.
PK parameters were not calculable for Subjects 34, 37, 39, and 138 on Day 28.

[0071] *Safety Results.* There were no deaths, serious adverse events (SAEs), or subject discontinuations due to AEs reported in this study. No trend was observed in single or multiple ascending doses of DS102 with regard to subject incidence for AE reporting and was comparable to AE reporting following placebo. The PI considered the majority of events to be mild in intensity and not related to the study treatment. The majority of the events reported were considered not related to the study treatment with events of dysguesia and eructation (following DS102 treatment) considered related. There were several laboratory events reported as AEs during the study in Parts 1 and 2. All laboratory reported events were mild in intensity and considered not related to the study treatment.

[0072] Single ascending doses of 100 mg, 500 mg, 1000 mg and 2000 mg DS102 and multiple ascending doses of 500 mg, 500 and 1000 mg were safe and well tolerated in the healthy subjects in this study.

[0073] PK profiles of 15(S)-HEPE in healthy subjects following single oral administration of 100 mg, 500 mg, 1000 mg, or 2000 mg DS102 and following multiple