## 1st Interim Analysis

Table 2. Population pharmacokinetic parameter estimates of bilastine after mixed effect modeling with NONMEM VI in children from group A (N=11, observations=60).

| MODEL: V-WT.CL-AGE.noX4.43.lst | | OBJ: 441.1 | |
|---|---|---|---|
| Parameter | Estimated | SEE | SEE% |
| KA (1/hr) | 1.28 | NA | NA |
| CLbase (L/hr) | 13.2 | 1.20 | 9.10 |
| V2base (L) | 19.0 | 4.34 | 22.8 |
| Q (L/hr) | 2.52 | 0.691 | 27.4 |
| V3 (L) | 16.9 | 2.45 | 14.5 |
| Tlag (hr) | 0.18 | 0.0524 | 29.1 |
| alpha | 0.41 | 0.302 | 74 |
| beta | 0.0 | NA | NA |
| ω_CL | 22% | 5% | 5% |
| ω_V2 | 60% | 40% | 44% |
| σ | 38% | 22% | 33% |

Note to Table 2. All parameters are scaled by bioavailability (F – not shown for clarity) so, e.g. CL should be understood as CL/F, etc. The Greek symbols Omega (ω) and sigma (σ) stand for inter-individual variability and for residual variability respectively, proportional standard deviations shown as percentages. Note that SEE% for the proportional variabilities is calculated for the variance. Parameters that are fixed have no estimation error (NA) (see also text).

## 2nd Interim Analysis:

Table 2. Population pharmacokinetic parameter estimates of bilastine after mixed effect modeling with NONMEM VI in children from group A and B (N=25, observations=89).

| MODEL: BILAS.ped.AnB1.B3.6.x.lst | | OBJ: 568.461 | |
|---|---|---|---|
| Parameter | Estimate | SEE | SEE% |
| KA (1/hr) | 1.49 | 0.214 | 14.4 |
| CL (L/hr) | 13.8 | 1.23 | 8.9 |
| V2 (L) | 24.6 | 3.78 | 15.4 |
| Q (L/hr) | 1.76 | 0.362 | 20.6 |
| V3 (L) | 16.3 | 1.9 | 11.7 |
| Tlag (hr) | 0.186 | 0.032 | 17.2 |
| ω_CL | 32% | 21% | 41% |
| ω_V2 | 51% | 34% | 44% |
| ω_Ka | 52.0 | 26% | 24% |
| ω_Tlag | 30% | 25% | 64% |
| σ | 23% | 11% | 23% |

Note to Table 2. All parameters are scaled by bioavailability (F – not shown, for clarity) so, e.g. CL should be understood as CL/F, etc. The Greek symbols Omega (ω) and sigma (σ) stand for inter-individual variability and for residual variability respectively, proportional standard deviations shown as percentages. Note that SEE% for the proportional variabilities (ω and σ) are calculated based on the corresponding variances.

**Final Model Analysis**

Table 3. *Final population pharmacokinetic parameter estimates of bilastine after mixed effect modeling with NONMEM in children from groups A and B (N=29, observations=91).*

| MODEL: bila-ped.all.4.3.1.4.lst | | OBJ: 597.7 | |
|---|---|---|---|
| **Parameter** | **Estimate** | **SEE** | **SEE%** |
| KA (1/hr) | 1.29 | 0.286 | 22.2 |
| CL (L/hr) | 12.5 | 0.74 | 5.9 |
| V2 (L) | 19.7 | 2.53 | 12.8 |
| Q (L/hr) | 2.01 | 0.684 | 34 |
| V3 (L) | 17.4 | 2.58 | 14.8 |
| Tlag (hr) | 0.183 | 0.0079 | 4.3 |
| ω_CL | 15% | 9% | 40% |
| ω_Ka | 67% | 37% | 30% |
| σ | 35% | 17% | 22% |

Note to Table 3. All parameters are scaled by bioavailability (F – not shown, for clarity) so, e.g. CL should be understood as CL/F, etc. The Greek symbols Omega (ω) and sigma (σ) stand for inter-individual variability and for residual variability respectively, proportional standard deviations shown as percentages. Note that SEE% for the proportional variabilities (ω and σ) are calculated based on the corresponding variances.