



|                                |  |                  |  |                                             |  |       |  |     |  |                            |  |
|--------------------------------|--|------------------|--|---------------------------------------------|--|-------|--|-----|--|----------------------------|--|
|                                |  | INR              |  | INR                                         |  | K     |  | INR |  |                            |  |
| HMG-CoA                        |  | INR              |  |                                             |  |       |  | CPK |  | 2 AUC C <sub>max</sub> 1.3 |  |
| C <sub>max</sub> 75mg 300mg    |  |                  |  | AUC <sub>0-4</sub> 20% C <sub>max</sub> 30% |  |       |  |     |  |                            |  |
| AUC / 26% 34%                  |  | HRT HRT          |  |                                             |  |       |  |     |  |                            |  |
|                                |  | HMG-CoA          |  |                                             |  |       |  |     |  |                            |  |
| 1                              |  | 1                |  | AUC                                         |  |       |  |     |  |                            |  |
| 1                              |  |                  |  | AUC                                         |  |       |  |     |  |                            |  |
| 75mg BID 200mg BID 6           |  | 10mg OD 10       |  | 7.1 ↑                                       |  |       |  |     |  |                            |  |
| 300mg/ 100mg OD 8              |  | 10mg             |  | 3.1 ↑                                       |  |       |  |     |  |                            |  |
| 160mg OD 14                    |  | 5mg              |  | 3.8 ↑                                       |  |       |  |     |  |                            |  |
| 100mg OD                       |  | 10mg             |  | 2.7 ↑                                       |  |       |  |     |  |                            |  |
| 25mg/ 400mg BID 14             |  | 150mg/ 100mg OD/ |  | 5mg                                         |  | 2.6 ↑ |  |     |  |                            |  |
| 200mg/ 50mg OD 11              |  | 10mg             |  | 2.3 ↑                                       |  |       |  |     |  |                            |  |
| 400mg/ 120mg OD 7              |  | 5mg OD 7         |  | 2.2 ↑                                       |  |       |  |     |  |                            |  |
| 400mg/ 100mg BID 17            |  | 20mg OD 7        |  | 2.1 ↑                                       |  |       |  |     |  |                            |  |
| 300mg 24 75mg                  |  | 20mg             |  | 2 ↑                                         |  |       |  |     |  |                            |  |
| 300mg 75mg OD 7                |  | 40mg OD          |  | 2 ↑ 1.4 ↑                                   |  |       |  |     |  |                            |  |
| 600mg BID 7                    |  | 80mg             |  | 1.9 ↑                                       |  |       |  |     |  |                            |  |
| 75mg OD 5                      |  | 10mg             |  | 1.6 ↑                                       |  |       |  |     |  |                            |  |
| 600mg/ 100mg BID 7             |  | 10mg OD 7        |  | 1.5 ↑                                       |  |       |  |     |  |                            |  |
| 500mg/ 200mg BID 11            |  | 10mg             |  | 1.4 ↑                                       |  |       |  |     |  |                            |  |
| 400mg BID                      |  |                  |  | 1.4 ↑                                       |  |       |  |     |  |                            |  |
| 200mg OD 5                     |  | 10mg             |  | **1.4 ↑                                     |  |       |  |     |  |                            |  |
| 700mg/ 100mg BID 8             |  | 10mg             |  | ↔                                           |  |       |  |     |  |                            |  |
| 0.3mg 7                        |  | 40mg 7           |  | ↔                                           |  |       |  |     |  |                            |  |
| 140mg TID 5                    |  | 10mg             |  | ↔                                           |  |       |  |     |  |                            |  |
| 67mg TID 7                     |  | 10mg 7           |  | ↔                                           |  |       |  |     |  |                            |  |
| 450mg QD 7                     |  | 20mg             |  | ↔                                           |  |       |  |     |  |                            |  |
| 200mg BID 7                    |  | 80mg             |  | ↔                                           |  |       |  |     |  |                            |  |
| 200mg OD 11                    |  | 80mg             |  | ↔                                           |  |       |  |     |  |                            |  |
| 500mg QID 7                    |  | 80mg             |  | 20% ↓                                       |  |       |  |     |  |                            |  |
| 50mg TID 14                    |  | 20mg             |  | 47% ↓                                       |  |       |  |     |  |                            |  |
| * X ↑ **                       |  |                  |  | %                                           |  |       |  |     |  |                            |  |
| OD = 1 BID = 2 TID = 3 QID = 4 |  |                  |  |                                             |  |       |  |     |  |                            |  |

|          |  |            |  |          |  |    |  |            |  |  |  |
|----------|--|------------|--|----------|--|----|--|------------|--|--|--|
| CK       |  |            |  |          |  |    |  |            |  |  |  |
| 40mg/ 15 |  | 56         |  | 50mg/ 14 |  | 18 |  | 5,000mg/kg |  |  |  |
|          |  | 3,000mg/kg |  |          |  |    |  |            |  |  |  |

|               |  |       |  |       |  |       |  |     |  |     |  |
|---------------|--|-------|--|-------|--|-------|--|-----|--|-----|--|
| LDL-C/HDL-C 2 |  | ApoB  |  | LDL   |  | HDL 2 |  | HDL |  | B   |  |
| N             |  | LDL-C |  | HDL-C |  | HDL   |  | B   |  | -A1 |  |
| 13            |  | -7    |  | -5    |  | 3     |  | -3  |  | 0   |  |
| 5             |  | 17    |  | -45   |  | -33   |  | 13  |  | -35 |  |
| 10            |  | 17    |  | -52   |  | -36   |  | 14  |  | -10 |  |
| 20            |  | 17    |  | -55   |  | -40   |  | 8   |  | -23 |  |
| 40            |  | 18    |  | -63   |  | -46   |  | 10  |  | -28 |  |
| 1             |  | 2     |  | 90%   |  | 4     |  |     |  |     |  |

|                                |  |            |  |                  |  |                  |  |         |  |       |  |
|--------------------------------|--|------------|--|------------------|--|------------------|--|---------|--|-------|--|
| HDL-C                          |  | ACS        |  | A D LDL-C        |  | 14C              |  |         |  |       |  |
|                                |  |            |  |                  |  |                  |  |         |  |       |  |
| AUC C <sub>max</sub> 10mg 10mg |  |            |  |                  |  |                  |  |         |  |       |  |
|                                |  | 5          |  | 20%              |  |                  |  |         |  |       |  |
| - 10mg                         |  | 1-2        |  | C <sub>max</sub> |  | 4-12             |  |         |  |       |  |
| 134L 90%                       |  |            |  | LDL-C            |  | 99.7% 88%-92%    |  |         |  |       |  |
| P450 N-                        |  | CYP2C9 N-  |  | HMG-CoA          |  | 2C19 3A4 2D6 50% |  |         |  |       |  |
|                                |  | II I       |  | 10%-20% 80%-90%  |  | -                |  | 22      |  |       |  |
| 90%                            |  | 5%         |  | 50L/h OATP-C     |  | 21.7% 19         |  | HMG-CoA |  |       |  |
| 14C-                           |  | 20mg       |  | 78% 11% 48       |  | 93% 10           |  |         |  |       |  |
|                                |  | Child-Pugh |  | Child-Pugh       |  | Child-Pugh       |  | 7 8 9 2 |  |       |  |
| AUC 10mg 10mg                  |  | 1.7        |  | 1                |  | 14               |  | AUC >9  |  | 14    |  |
| n=9                            |  | N-         |  | CrCl<30ml/min    |  | N-               |  |         |  |       |  |
| 12                             |  | 1          |  | 50%              |  | 1.5              |  | 10mg    |  |       |  |
| ≥ 65 LDL-C                     |  |            |  | 20%              |  | 18-45            |  | 2       |  | LDL-C |  |
| 10-17 6-17                     |  |            |  |                  |  | 214              |  | 2       |  |       |  |

|                                                                     |                  |                          |  |                               |  |                                     |                  |                                                          |  |                              |  |
|---------------------------------------------------------------------|------------------|--------------------------|--|-------------------------------|--|-------------------------------------|------------------|----------------------------------------------------------|--|------------------------------|--|
| HoFH HeFH                                                           |                  |                          |  |                               |  |                                     |                  |                                                          |  |                              |  |
| AUC                                                                 | C <sub>max</sub> | 2                        |  | -                             |  | AUC                                 | C <sub>max</sub> | 1.3                                                      |  |                              |  |
| HMG-CoA<br>OATP1B1 / ABCG2 BCRP<br>c.521CC ABCG2 c.421AA<br>c.421CC |                  |                          |  |                               |  | OATP1B1 BCRP<br>AUC SLCO1B1 c.521TT |                  | SLCO1B1<br>SLCO1B1<br>c.521TT ABCG2                      |  |                              |  |
| LDL-C<br>80%                                                        |                  | III<br>4.8mmol/L<br>10mg |  | LDL-C<br>LDL-C                |  | EAS                                 |                  | IIa IIb<br>EAS 1998<br><3mmol/L                          |  |                              |  |
| 20mg<br>40mg                                                        |                  | 80mg<br>12               |  | 435<br>LDL-C                  |  | 53%<br>33%                          |                  | 42<br>EAS                                                |  | LDL-C<br><3mmol/l            |  |
| 20-40mg                                                             |                  |                          |  |                               |  |                                     |                  | LDL-C                                                    |  | 22%                          |  |
|                                                                     |                  | LDL-C<br>HDL-C           |  | B ApoB                        |  | TG                                  |                  |                                                          |  |                              |  |
| 8                                                                   |                  | NCEP LDL-C               |  | 2.6-4.1mmol/l/[100-160 mg/dL] |  | 10mg                                |                  |                                                          |  |                              |  |
| LDL-C                                                               |                  |                          |  | LDL-C<br>vs.                  |  | ~82%                                |                  | 10mg                                                     |  | 72% 19%                      |  |
| 2                                                                   |                  | 1,719<br>10mg            |  | 13%<br>LDL-C(19%)<br>A D E    |  | ApoB 14%                            |                  | TG 8%                                                    |  | HDL-C                        |  |
| 3%                                                                  |                  | /                        |  |                               |  |                                     |                  |                                                          |  |                              |  |
| 469                                                                 |                  | 10mg                     |  | LDL-C                         |  |                                     |                  | LDL-C                                                    |  | 6                            |  |
| mmol/L vs. 2.8mmol/L                                                |                  | /                        |  | LDL                           |  | p 0.001                             |                  | /                                                        |  | 3.4                          |  |
| 6                                                                   |                  | 10mg                     |  | 5mg                           |  | 10mg                                |                  | 10mg                                                     |  | 20mg                         |  |
| mg/dL                                                               |                  | 440 /                    |  | <100mg/dL                     |  |                                     |                  | III                                                      |  | <70                          |  |
| 5.7%                                                                |                  | LDL-C                    |  | 21%                           |  | 5mg                                 |                  | 10mg                                                     |  | 10mg                         |  |
| 10mg                                                                |                  | LDL-C                    |  | 20mg                          |  | LDL-C                               |                  | 10mg                                                     |  | 20mg                         |  |
| 5 mg<br>452                                                         |                  | 10mg<br>LPS15021         |  | 10mg<br>CVD                   |  | HR                                  |                  | VHR                                                      |  | 10 mg 20 mg                  |  |
| 6                                                                   |                  | 208 HR                   |  | 10mg/<br>n=104                |  | 10mg                                |                  | LMT                                                      |  |                              |  |
| =104                                                                |                  | 244 VHR                  |  | 20mg(R20 n=79)                |  | 10mg FDC R20/E10 n=82               |                  | FDC R20/E10 n=83                                         |  | FDC (R10/E10 n=82)           |  |
| 40mg/<br>VHR                                                        |                  | 10mg FDC R40/E10 n=79    |  | mITT                          |  | 6 LS                                |                  | R40                                                      |  | -34.28% R20/E10 LS           |  |
| -26.90% R40                                                         |                  | R40/E10                  |  | LDL-C                         |  | R20/E10                             |                  | R10/E10                                                  |  | LS                           |  |
| -19.66% HR                                                          |                  | p<0.001                  |  | FDC                           |  | 6 LDL-C R20                         |                  | R10/E10                                                  |  | -27.02% p                    |  |
| R20 =0.306                                                          |                  | -21.82%                  |  | R10/E10                       |  | R10/E10                             |                  | LDL-C                                                    |  | HR                           |  |
| R10/E10                                                             |                  | LS                       |  | R10/E10                       |  | R20 -8.84%                          |                  | p=0.026                                                  |  |                              |  |
| R10                                                                 |                  | R10/E10FDC8              |  | LDL-C                         |  | III                                 |                  |                                                          |  | /                            |  |
| R10/E10                                                             |                  | 305<br>1 0.7%            |  |                               |  | R10/E10                             |                  | 153                                                      |  | R10 152                      |  |
|                                                                     |                  | LMT                      |  | 10mg                          |  | R10                                 |                  | R10/E10                                                  |  | LDL-C                        |  |
| -13.85% p<0.0001                                                    |                  | R10                      |  | 8                             |  | R10/E10                             |                  | LDL-C                                                    |  | 8                            |  |
| -21.98% R10                                                         |                  | -8.12%                   |  | 29.2%                         |  | R10/E10                             |                  | LDL-C-2.6mmol/L                                          |  | 100mg/dL                     |  |
| 54.1%                                                               |                  |                          |  |                               |  | OR                                  |                  | 2.80 p<0.0001                                            |  |                              |  |
|                                                                     |                  | LDL-C                    |  | B Apo B<br>HDL-C              |  | TG                                  |                  |                                                          |  | T-C<br>non-HDL-C             |  |
|                                                                     |                  | HMG-CoA                  |  | 3-                            |  | -3-<br>LDL                          |                  | A                                                        |  | LDL                          |  |
| VLDL                                                                |                  | VLDL                     |  | LDL                           |  |                                     |                  |                                                          |  |                              |  |
| Niemann-Pick C1-like 1 (NPC1L1)                                     |                  |                          |  |                               |  |                                     |                  |                                                          |  |                              |  |
| Ames                                                                |                  |                          |  |                               |  |                                     |                  |                                                          |  |                              |  |
| Ames                                                                |                  |                          |  |                               |  |                                     |                  |                                                          |  |                              |  |
| 7<br>10mg/                                                          |                  | 30                       |  | 5 15 50mg/kg/                 |  | 50mg/kg/                            |                  | 9<br>1                                                   |  | 2                            |  |
| 40                                                                  |                  | Spermatidic giant cell   |  |                               |  | 6                                   |                  | AUC                                                      |  | 30mg/kg/<br>10mg/            |  |
|                                                                     |                  |                          |  |                               |  |                                     |                  | 16                                                       |  | 25mg/kg                      |  |
|                                                                     |                  | 1mg/kg                   |  | 5 15 50mg/kg/                 |  | 50mg/kg/                            |                  | 3% 20% 25%<br>AUC                                        |  | 18 2                         |  |
| 7<br>10mg/<br>mg/kg/                                                |                  | 30                       |  | 3 4                           |  | 3mg/kg/                             |                  | 7                                                        |  | 25                           |  |
| 10 50mg/kg/                                                         |                  | 10mg/                    |  | 50mg/kg/                      |  | 18 4                                |                  | 0.3 1 3mg/kg/                                            |  | 21 48<br>3mg/kg/             |  |
| 10mg/                                                               |                  | 6                        |  | 1000mg/kg/                    |  |                                     |                  | AUC <sub>0-24hr</sub>                                    |  | 1000mg/kg/                   |  |
| 10mg/                                                               |                  | 15                       |  | 7                             |  | 19                                  |                  | 10mg/                                                    |  | 250 500 1000mg/kg/<br>10 150 |  |
| 22                                                                  |                  | 10mg/                    |  | 6 134<br>1000mg/kg/           |  | -                                   |                  |                                                          |  | NOEL<br>20 0.03              |  |
| 0.5<br>AUC <sub>0-24hr</sub>                                        |                  | 6                        |  | 21<br>10mg/                   |  | 17                                  |                  | 100 300 1000mg/kg/                                       |  |                              |  |
| AUC                                                                 |                  | 104                      |  | 10mg/                         |  | 60<br>107                           |                  | 2 20 60 80mg/kg/                                         |  | 80mg/kg/                     |  |
| 200mg/kg/                                                           |                  | 200mg/kg/<br>/           |  | AUC                           |  |                                     |                  | 10mg/<br>/                                               |  | 60 10 60                     |  |
| 500mg/kg/                                                           |                  | 104                      |  | AUC <sub>0-24hr</sub>         |  | 10mg/                               |                  | 1500mg/kg/<br>20                                         |  | 104                          |  |
| 150                                                                 |                  | 500mg/kg/                |  |                               |  | AUC <sub>0-24hr</sub>               |                  | 10mg/                                                    |  | 10mg/                        |  |
| CNS                                                                 |                  |                          |  |                               |  |                                     |                  |                                                          |  |                              |  |
| 1<br>300<br>6mg/kg/<br>12                                           |                  | 24<br>AUC                |  | Wallerian<br>90mg/kg/         |  | AUC                                 |                  | 30                                                       |  | 10mg/                        |  |
| 10mg/                                                               |                  | 300                      |  | 30mg/kg/                      |  | 10mg/<br>AUC                        |                  | 60                                                       |  | 52<br>10mg/                  |  |
| 7 /<br>18                                                           |                  | 10mg/<br>30<br>/ /       |  | 180                           |  | 1                                   |                  | 30mg/kg/                                                 |  | AUC                          |  |
| H20263565                                                           |                  |                          |  |                               |  | YBH03482026                         |                  |                                                          |  |                              |  |
| 210038<br>025-85109999<br>025-85803122<br>www.njcttq.com            |                  | 9                        |  |                               |  |                                     |                  | 210038<br>025-85109999<br>025-85803122<br>www.njcttq.com |  | 9                            |  |