

| Mut   | BAM | ETE | CAS | IMD | CIL | TIX | SOT | BEB | REG | AMU | ROM | ADI | C135 | C144 | in patient | in vitro | Prevalence |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------------|----------|------------|
| P337H |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 1          |          | 0.0008%    |
| P337L |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 3          | 1        | 0.003%     |
| P337R |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 2          |          | 0.0004%    |
| P337S |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 6          |          | 0.003%     |
| P337T |     |     |     |     |     |     | +   |     |     |     |     |     |      |      |            |          | 0.001%     |
| E340A |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 5          | 3        | 0.002%     |
| E340D |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 8          |          | 0.003%     |
| E340G |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 1          |          | 0.0008%    |
| E340K |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 8          | 1        | 0.004%     |
| E340Q |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 2          |          | 0.0005%    |
| E340V |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 3          |          | 0.001%     |
| T345P |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 1          |          | 0.0001%    |
| R346G |     |     |     |     |     | +   |     |     |     |     |     |     | +    |      | 4          |          | 0.005%     |
| R346I |     |     |     |     |     | +   |     |     |     |     |     |     | +    |      | 1          | 3        | 0.01%      |
| R346K |     |     |     |     |     |     |     |     |     |     |     |     | +    |      | 2          |          | 9%         |
| R346S |     |     |     |     |     |     |     |     |     |     |     |     | +    |      | 1          | 1        | 0.03%      |
| R346T |     |     |     |     |     |     |     |     |     |     |     |     | +    |      | 1          |          |            |
| K356E |     |     |     |     |     |     | +   |     |     |     |     |     |      |      |            |          | 0.002%     |
| K356Q |     |     |     |     |     |     | +   |     |     |     |     |     |      |      |            |          | 0.001%     |
| K356T |     |     |     |     |     |     | +   |     |     |     |     |     |      |      | 1          |          | 0.0008%    |
| S366P |     |     |     |     |     |     |     | +   |     |     |     |     |      |      |            |          | 0.0002%    |
| S366T |     |     |     |     |     |     |     | +   |     |     |     |     |      |      |            |          | 0.0001%    |
| S371F |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 2          |          | 6%         |
| S371L |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 1          |          | 17%        |
| D405E |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.0005%    |
| D405N |     | +   |     |     |     |     |     |     |     |     |     |     |      |      | 1          |          | 6%         |
| E406D |     |     |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.001%     |
| R408K |     |     |     |     |     |     |     | +   |     |     |     |     |      |      | 1          |          | 0.005%     |
| K417E |     | +   | +   |     |     |     |     |     |     |     |     |     |      |      | 9          |          | 0.0004%    |
| K417H |     | +   | +   |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.0002%    |
| K417I |     | +   | +   |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.0002%    |
| K417M |     | +   | +   |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.0003%    |
| K417N |     | +   |     |     |     |     |     |     |     |     |     |     |      |      | 1          | 6        | 23%        |
| K417R |     |     | +   |     |     |     |     |     |     |     |     |     |      |      | 2          |          | 0.004%     |
| K417S |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.0002%    |
| K417T |     | +   |     |     |     |     |     |     |     |     |     |     |      |      | 1          | 1        | 1%         |
| D420A |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.0002%    |
| D420N |     | +   |     |     |     |     |     |     |     |     |     |     |      |      | 1          |          | 0.0008%    |
| N439K |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 2          |          | 0.6%       |
| N440D |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          | 2        | 0.0004%    |
| N440E |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.0001%    |
| N440I |     |     |     | +   |     |     |     |     |     |     |     |     | +    |      |            |          | 0.0006%    |
| N440K |     |     |     | +   |     |     |     |     |     |     |     |     | +    |      | 2          | 2        | 23%        |
| N440R |     |     |     |     |     |     |     |     |     |     |     |     | +    |      |            |          | 0.0002%    |
| N440T |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.001%     |
| N440Y |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.004%     |
| S443Y |     |     |     | +   |     |     |     |     |     |     |     |     | +    |      |            |          | 0.0001%    |
| K444E |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      | 7          |          | 0.0002%    |
| K444F |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      |            |          | 0.0001%    |
| K444I |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      |            |          | 0.0002%    |
| K444L |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      |            |          | 0.0001%    |
| K444M |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      |            |          | 0.001%     |
| K444N |     |     |     | +   | +   |     |     | +   |     |     |     |     |      |      | 6          |          | 0.01%      |
| K444R |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 5          |          | 0.01%      |
| K444T |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      | 3          |          | 0.002%     |
| V445A |     |     |     | +   | +   |     |     | +   |     |     |     |     |      |      | 4          |          | 0.005%     |
| V445D |     | +   |     | +   | +   |     |     | +   |     |     |     |     |      |      |            |          | 0.0001%    |
| V445F |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          |          | 0.003%     |

| Mut   | BAM | ETE | CAS | IMD | CIL | TIX | SOT | BEB | REG | AMU | ROM | ADI | C135 | C144 | in patient | in vitro | Prevalence |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------------|----------|------------|
| V445I |     |     |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.003%     |
| V445L |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.0002%    |
| G446A |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.001%     |
| G446D |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 4          |          | 0.001%     |
| G446I |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      |            |          | 0.0001%    |
| G446N |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.0008%    |
| G446R |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          |          | 0.002%     |
| G446S |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 17%        |
| G446T |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.0001%    |
| G446V |     |     |     | +   |     |     |     |     |     |     |     |     | +    |      | 4          | 4        | 0.1%       |
| G447C |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      |            |          | 0.0001%    |
| G447D |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      |            |          | 0.0002%    |
| G447F |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      |            |          | 0.0001%    |
| G447S |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      | 1          |          | 0.0007%    |
| G447V |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      |            |          | 0.001%     |
| N448D |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      | 1          |          | 0.0005%    |
| N448K |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      |            |          | 0.0006%    |
| N448T |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      |            |          | 0.0006%    |
| N448Y |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      |            |          | 0.0001%    |
| Y449D |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      |            |          | 0.0007%    |
| N450D |     |     |     |     | +   |     |     |     |     |     |     |     |      |      | 1          | 5        | 0.002%     |
| N450K |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 2          |          | 0.03%      |
| L452M |     |     |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.03%      |
| L452Q |     |     |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.1%       |
| L452R |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 2          | 6        | 38%        |
| L452W |     |     |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.002%     |
| Y453F |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          | 3        | 0.03%      |
| Y453H |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.0003%    |
| L455F |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          | 2        | 0.03%      |
| L455M |     |     |     | +   | +   |     |     | +   |     |     |     |     |      |      |            |          | 0.0001%    |
| L455S |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      |            |          | 0.002%     |
| L455W |     |     |     | +   | +   |     |     |     |     |     |     |     | +    |      | 1          |          | 0.0001%    |
| F456C |     |     |     | +   |     |     |     |     |     |     |     |     | +    |      |            |          | 0.0002%    |
| F456L |     |     |     | +   |     |     |     |     |     |     |     |     | +    |      | 1          | 1        | 0.005%     |
| F456V |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 3          |          | 0.0004%    |
| S459P |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.0004%    |
| N460H |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          |          | 0.0001%    |
| N460I |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.001%     |
| N460K |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          | 1        | 0.002%     |
| N460S |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.01%      |
| N460T |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          |          | 0.0003%    |
| N460Y |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          |          | 0.001%     |
| I472F |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.0002%    |
| I472T |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          | 0.001%     |
| A475D |     |     |     | +   | +   |     | +   |     |     |     |     |     |      |      | 1          |          | 0.0001%    |
| A475V |     |     |     | +   | +   |     |     |     |     |     |     |     |      |      | 2          |          | 0.03%      |
| G476D |     |     |     | +   |     |     | +   |     |     |     |     |     |      |      | 1          | 7        | 0.0007%    |
| G476R |     |     |     | +   | +   |     | +   |     |     |     |     |     |      |      |            |          | 0.0001%    |
| G476S |     |     |     | +   |     |     |     |     |     |     |     |     |      |      | 1          | 4        | 0.02%      |
| G476T |     |     |     | +   | +   |     | +   |     |     |     |     |     |      |      |            |          | 0.0001%    |
| V483A |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 1          |          | 0.005%     |
| V483G |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 1          |          | 0.0003%    |
| E484A |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 2          | 4        | 23%        |
| E484D |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 1          | 5        | 0.003%     |
| E484G |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 1          | 3        | 0.003%     |
| E484K |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 26         | 33       | 3%         |
| E484P |     |     |     |     |     |     |     |     |     |     |     |     |      |      |            |          | 0.0008%    |
| E484Q |     |     |     |     |     |     |     |     |     |     |     |     |      |      | 11         | 1        | 0.2%       |

| Mut   | BAM | ETE | CAS | IMD | CIL | TIX | SOT | BEB | REG | AMU | ROM | ADI | C135 | C144 | in patient | in vitro | Prevalence |         |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------------|----------|------------|---------|
| E484R | +   |     |     |     |     |     |     |     |     |     |     |     |      |      | +          |          | 0.0005%    |         |
| E484S | +   |     |     |     |     |     |     |     |     |     |     |     |      |      | +          |          | 0.0008%    |         |
| E484T | +   |     | +   |     |     |     |     |     |     |     |     |     |      |      | +          |          | 0.0007%    |         |
| E484V | +   |     | +   |     |     |     |     |     |     |     |     |     |      |      | +          | 1        | 2          | 0.01%   |
| G485A | +   |     |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.002%  |
| G485D | +   |     | +   |     |     | +   |     |     |     |     |     |     |      |      |            | 3        |            | 0.0009% |
| G485R | +   |     |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.001%  |
| G485S | +   |     |     |     |     |     |     |     |     |     |     |     |      |      |            | 2        |            | 0.002%  |
| F486D | +   |     | +   |     |     | +   |     |     |     |     |     |     |      |      |            |          |            | 0.0001% |
| F486I | +   |     | +   |     |     | +   |     |     |     |     |     |     |      |      |            | 1        | 1          | 0.001%  |
| F486L | +   |     | +   |     |     |     |     |     |     |     |     |     |      |      |            | 2        |            | 0.002%  |
| F486N | +   |     | +   |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0001% |
| F486P | +   | +   | +   |     |     | +   |     |     |     |     |     |     |      |      | +          | 1        |            | 0.0002% |
| F486S |     | +   | +   |     |     | +   |     |     |     |     |     |     |      |      | +          | 6        |            | 0.003%  |
| F486T | +   | +   | +   |     |     | +   |     |     |     |     |     |     |      |      |            |          |            | 0.0001% |
| F486V | +   | +   | +   |     |     | +   |     |     |     |     |     |     |      |      |            | 9        |            | 0.0007% |
| N487D |     | +   | +   |     |     |     |     |     |     |     |     |     |      |      | +          | 3        |            | 0.0001% |
| N487H |     | +   |     |     |     | +   |     |     |     | +   |     |     |      |      |            |          |            | 0.0001% |
| N487S |     | +   | +   |     |     | +   |     |     |     |     |     |     |      |      |            | 1        |            | 0.0002% |
| Y489C |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0002% |
| Y489H |     | +   | +   |     |     | +   |     |     |     |     |     |     |      | +    | 1          |          |            | 0.001%  |
| Y489R |     | +   | +   |     |     | +   |     |     |     |     |     |     |      |      |            |          |            | 0.0002% |
| Y489W |     | +   | +   |     |     | +   |     |     |     |     |     |     |      |      |            |          |            | 0.0001% |
| F490G | +   |     |     |     |     |     |     |     |     |     |     |     |      |      | +          |          |            | 0.0001% |
| F490I |     |     |     |     |     |     |     |     |     |     |     |     |      |      | +          |          |            | 0.0007% |
| F490L | +   |     |     |     |     |     |     |     |     |     |     |     |      |      | +          | 3        | 4          | 0.02%   |
| F490R | +   |     |     |     |     |     |     |     |     |     |     |     |      |      | +          |          |            | 0.002%  |
| F490S | +   |     |     |     |     |     |     |     |     |     |     |     |      |      |            | 2        | 5          | 0.2%    |
| F490V |     |     |     |     |     |     |     |     |     |     |     |     |      |      | +          |          | 2          | 0.003%  |
| F490Y | +   |     |     |     |     |     |     |     |     |     |     |     |      |      |            | 1        |            | 0.002%  |
| Q493D | +   |     | +   |     |     |     |     |     |     |     |     |     |      |      | +          |          |            | 0.0002% |
| Q493E |     |     | +   |     |     |     |     |     |     |     |     |     |      |      |            | 1        |            | 0.009%  |
| Q493H | +   |     | +   |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.001%  |
| Q493K | +   | +   |     |     |     |     |     |     |     |     |     |     |      |      | +          | 3        | 8          | 0.002%  |
| Q493L | +   |     | +   |     |     |     |     |     |     |     |     |     |      |      | +          | 1        |            | 0.003%  |
| Q493R | +   | +   | +   |     |     |     |     |     |     |     |     |     |      |      | +          | 14       | 6          | 23%     |
| Q493V |     | +   | +   |     |     |     |     |     |     |     |     |     |      |      | +          |          |            | 0.0002% |
| S494P | +   |     |     |     |     |     |     |     |     |     |     |     |      |      | +          | 10       | 3          | 0.2%    |
| S494R | +   |     |     |     | +   |     |     |     |     |     |     |     |      |      |            |          |            | 0.0001% |
| G496S |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          |            | 17%     |
| Q498H |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0004% |
| P499H |     |     |     |     |     |     |     |     |     |     |     |     |      |      |            | 2        |            | 0.001%  |
| P499R |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            | 2        |            | 0.008%  |
| P499S |     |     | +   |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.003%  |
| P499T |     |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0007% |
| N501T |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            | 8        | 1          | 0.08%   |
| N501Y |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            | 5        | 3          | 45%     |
| G504C |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0001% |
| G504D |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            | 6        |            | 0.001%  |
| G504I |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0002% |
| G504L |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0001% |
| G504N |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0006% |
| G504R |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0001% |
| G504V |     | +   |     |     |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0006% |
| P507A | +   |     |     | +   |     |     |     |     |     |     |     |     |      |      |            |          |            | 0.0005% |
| C525A |     |     |     |     |     |     |     | +   |     |     |     |     |      |      |            |          |            | 0.0002% |