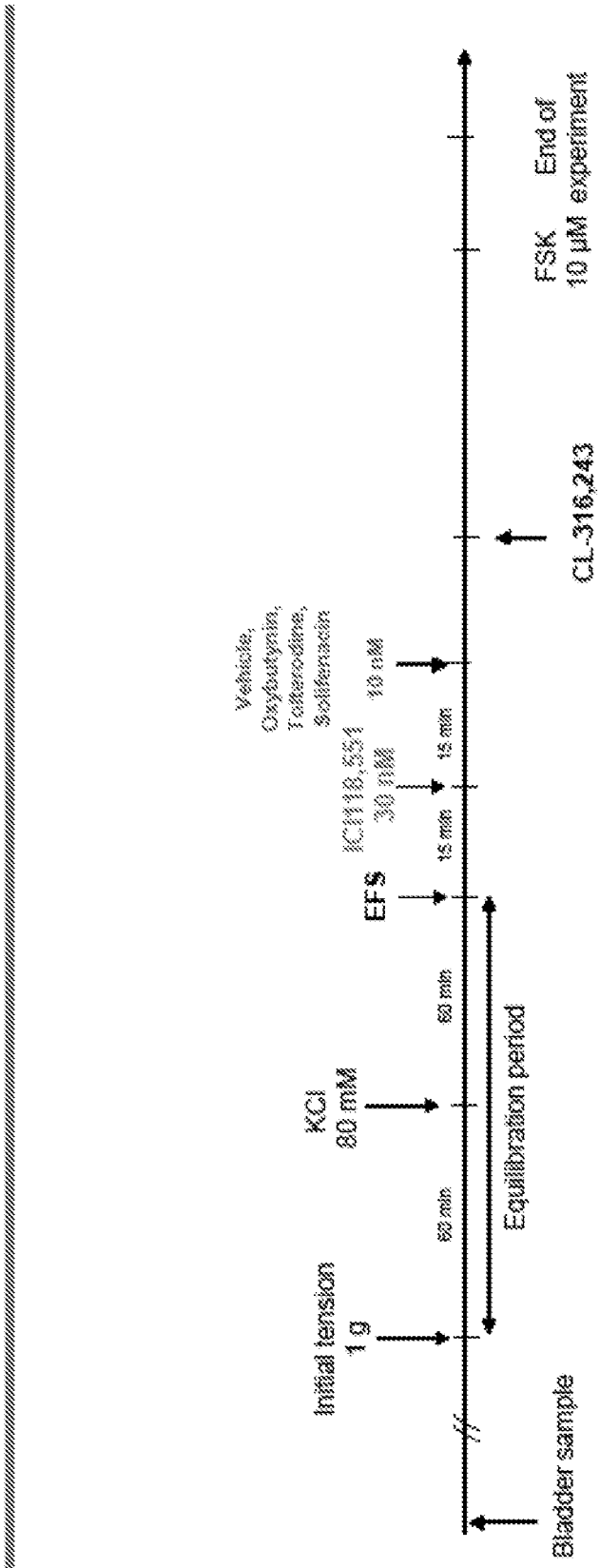

Experimental protocol
Initial tension
1 g
60 min
KCl
80 mM
60 min
Equilibration period
EFS
15 min
IC3118,551
30 nM
15 min
Vehicle,
Oxybutynin,
Tolterodine,
Solifenacin
10 nM
15 min
CL_316,243
Solabegron,
Mirabegron,
CRC 's
FSK
10 µM
End of
experiment
Bladder sample

FIGURE 1

## Effects of antimuscarinics alone on EFS-induced contractions in the different groups (% inhibition from basal)

| | Vehicle | Oxybutynin 10 nM | Tolterodine 10 nM | Solifenacin 10 nM |
|---|---|---|---|---|
| CL-316,243 | 5.87 ± 0.22 % (n=2) | 29.39 ± 14.50 % (n=2) | 39.10 ± 4.99 % (n=5) | 10.73 ± 2.00 % (n=5) |
| Solabegron | 6.75 ±1.36 % (n=5) | 18.96 ± 1.83 % (n=5) | 22.70 ± 4.75 % (n=5) | 10.40 ± 1.38 % (n=5) |
| Mirabegron | 9.06 ± 1.65 % (n=5) | 17.85 ± 1.05 % (n=5) | 32.29 ± 3.16 % (n=5) | 9.51 ± 4.02 % (n=5) |

FIGURE 2

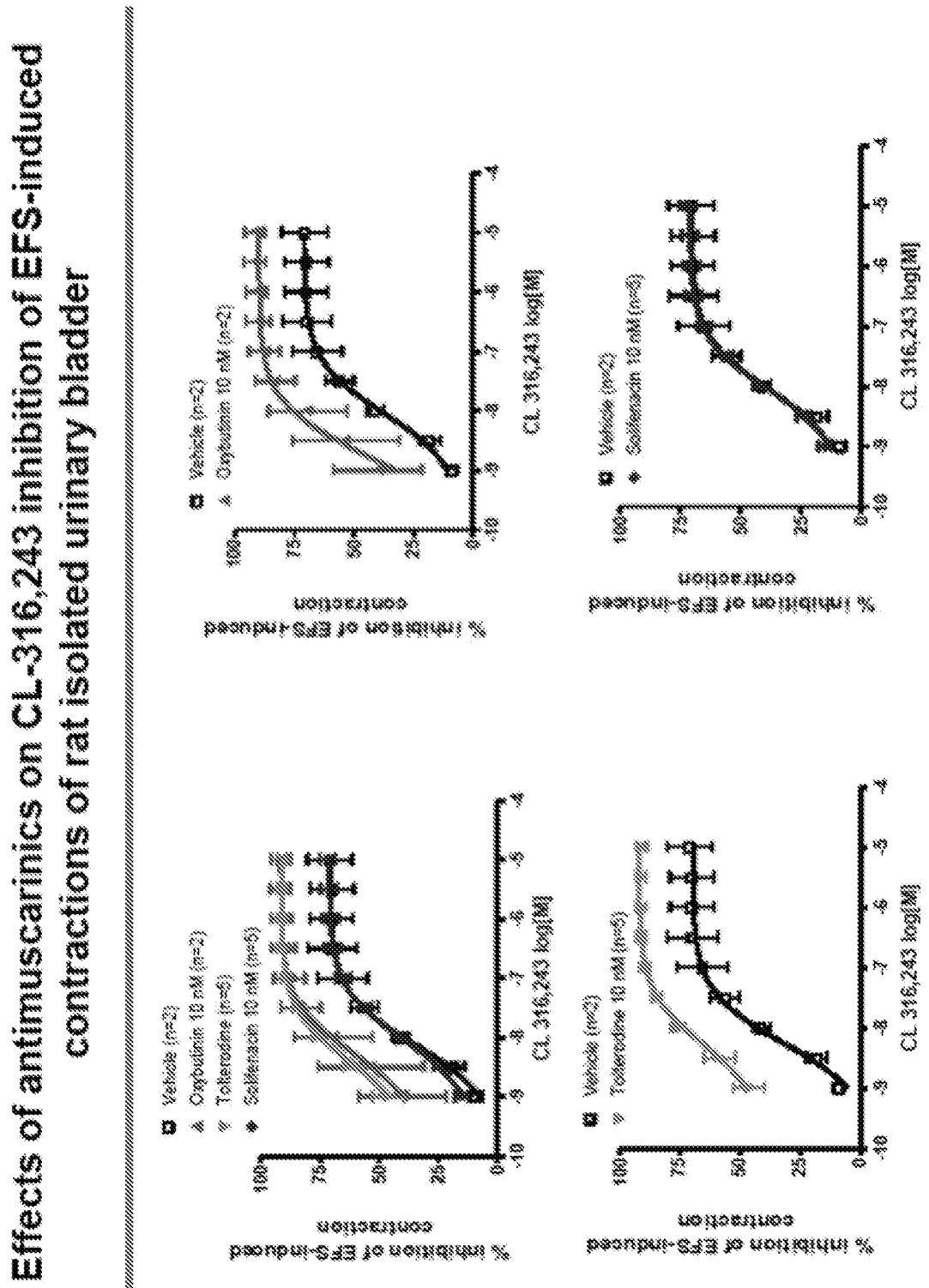

Effects of antimuscarinics on CL-316,243 inhibition of EFS-induced contractions of rat isolated urinary bladder
Vehicle (n=3)
Oxybutinin 10 nM (n=3)
Tolterodine (n=5)
Solifenacin 10 nM (n=5)
% inhibition of EFS-induced contraction
CL 316,243 log[M]

FIGURE 3

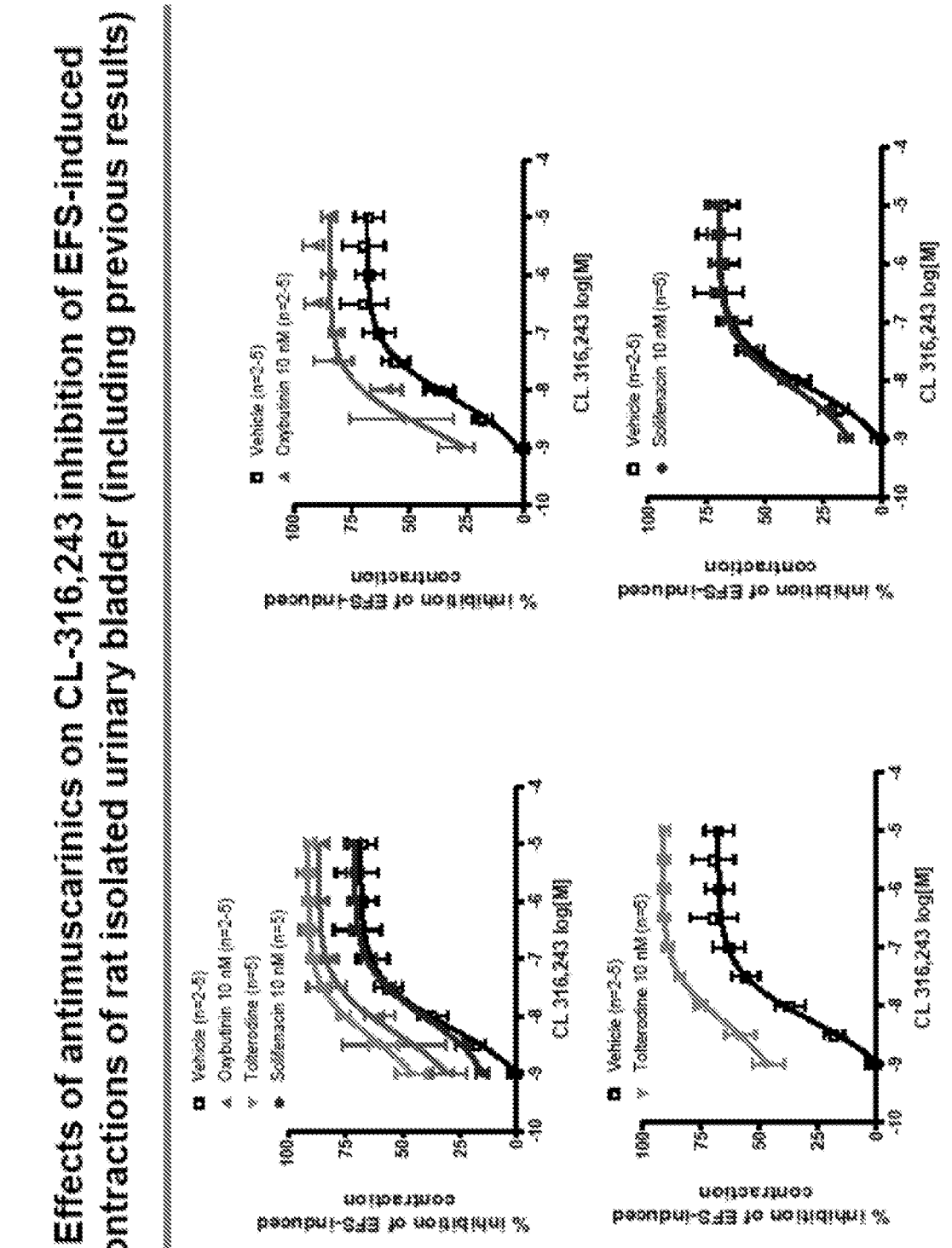

Effects of antimuscarinics on CL-316,243 inhibition of EFS-induced contractions of rat isolated urinary bladder (including previous results)
Vehicle (n=2-5)
Oxybutinin 10 nM (n=2-5)
Tolterodine (n=5)
Solifenacin 10 nM (n=5)
% inhibition of EFS-induced contraction
CL 316,243 log[M]

FIGURE 4

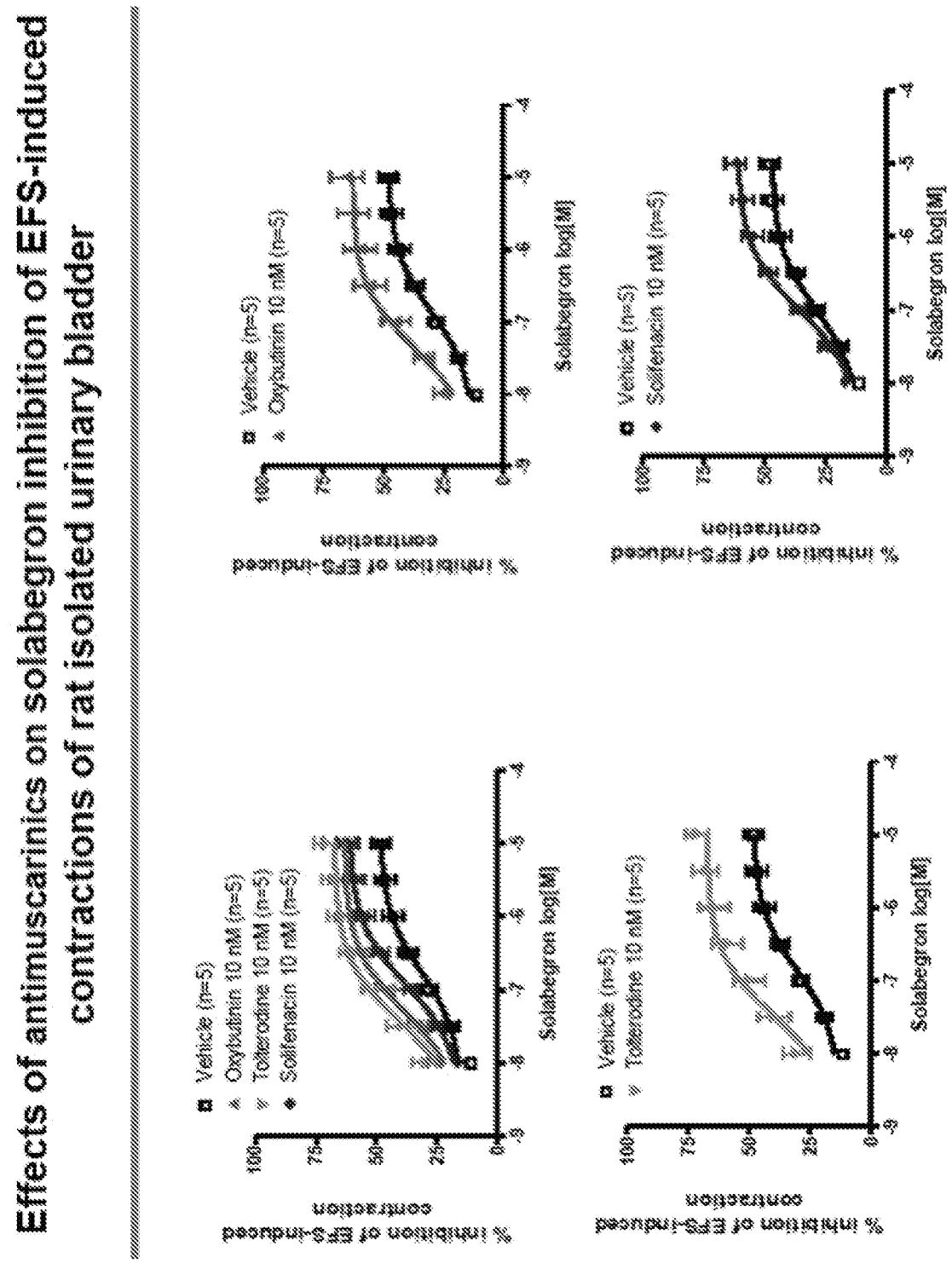

Effects of antimuscarinics on solabegron inhibition of EFS-induced contractions of rat isolated urinary bladder
Vehicle (n=5)
Oxybutinin 10 nM (n=5)
Tolterodine 10 nM (n=5)
Solifenacin 10 nM (n=5)
% inhibition of EFS-induced contraction
Solabegron log[M]

FIGURE 5

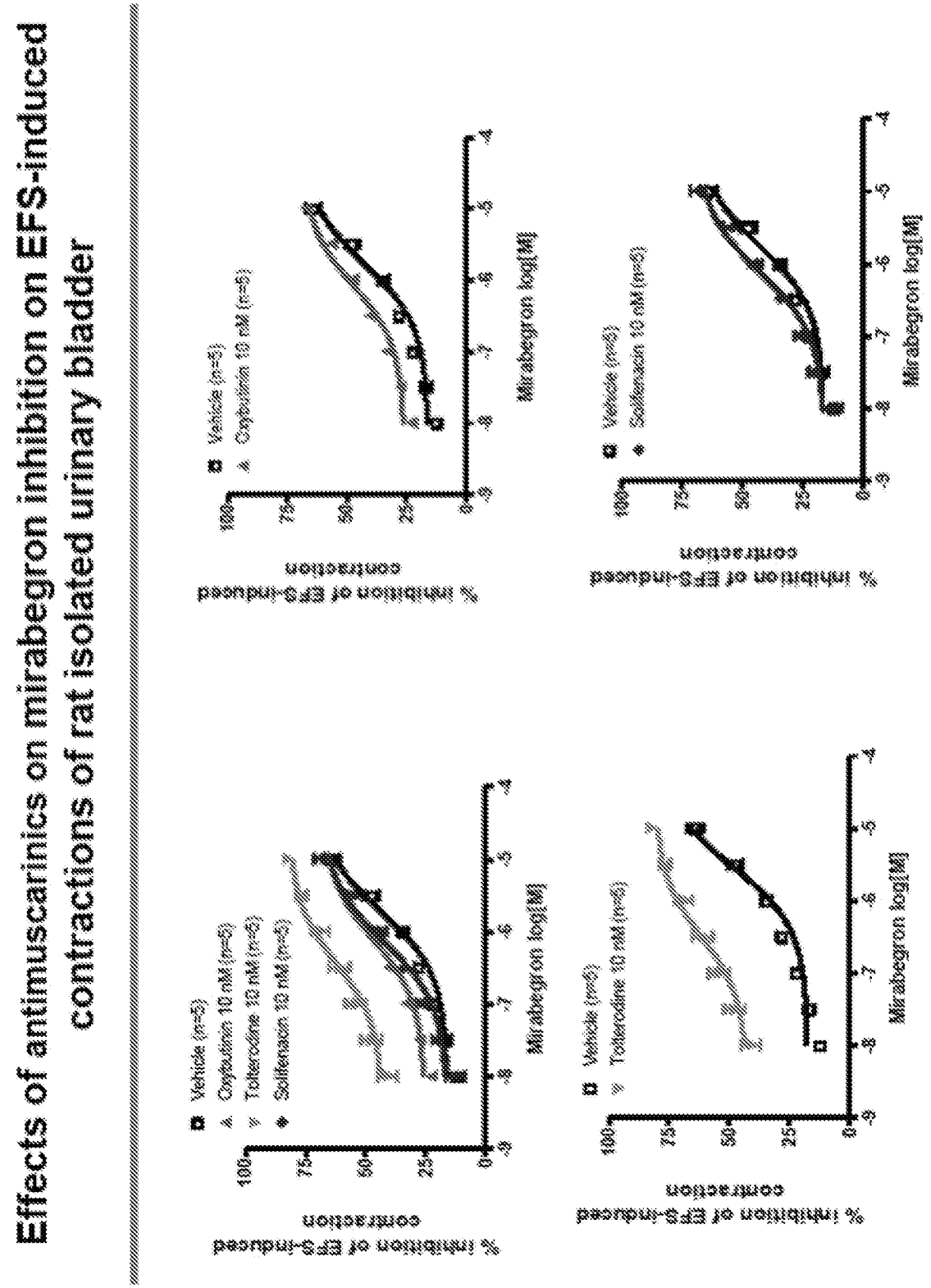

Effects of antimuscarinics on mirabegron inhibition on EFS-induced contractions of rat isolated urinary bladder
Vehicle (n=5)
Oxybutinin 10 nM (n=5)
Tolterodine 10 nM (n=5)
Solifenacin 10 nM (n=5)
% inhibition of EFS-induced contraction
Mirabegron log[M]

FIGURE 6

# $E_{max}$ and $pIC_{50}$ values

| | Vehicle | Oxybutynin 10 nM | Tolterodine 10nM | Solifenacin 10 nM |
|---|---|---|---|---|
| CL-316,243 | $E_{max}$ = 71.0 ± 3.9 %<br>$pIC_{50}$ = 8.0 ±0.2 | $E_{max}$ = 89.9* ± 3.4 %<br>$pIC_{50}$ = 8.7* ± 0.2 | $E_{max}$ = 91.3* ± 1.5 %<br>$pIC_{50}$ = 8.4 ± 0.2 | $E_{max}$ = 70.9 ± 1.5 %<br>$pIC_{50}$ = 8.1 ± 0.1 |
| Solabegron | $E_{max}$ = 48.3 ± 3.3 %<br>$pIC_{50}$ = 6.8 ± 0.3 | $E_{max}$ = 63.0* ± 2.7 %<br>$pIC_{50}$ = 7.3* ± 0.2 | $E_{max}$ = 67.1* ± 2.6 %<br>$pIC_{50}$ = 7.5* ± 0.1 | $E_{max}$ = 60.6* ± 2.1 %<br>$pIC_{50}$ = 7.0 ± 0.1 |
| Mirabegron | $E_{max}$ = 71.5 ± 4.9 %<br>$pIC_{50}$ = 5.8 ± 0.1 | $E_{max}$ = 68.2 ± 2.3 %<br>$pIC_{50}$ = 6.1* ± 0.1 | $E_{max}$ = 81.9 ± 3.1 %<br>$pIC_{50}$ = 6.5* ± 0.2 | $E_{max}$ = 68.5 ± 3.2 %<br>$pIC_{50}$ = 6.1* ± 0.1 |

*(*): $p < 0.05$ versus vehicle group*

**FIGURE 7**

# $E_{max}$ and $IC_{50}$ values

| | Vehicle | Oxybutynin 10 nM | Tolterodine 10nM | Solifenacin 10 nM |
|---|---|---|---|---|
| CL-316,243 | $E_{max}$ = 68.6 ± 3.0 %<br>$IC_{50}$ = 7.36 nM | $E_{max}$ = 84.7* ± 2.7 %<br>$IC_{50}$ = 1.91* nM | $E_{max}$ = 91.3* ± 1.5 %<br>$IC_{50}$ = 4.17 nM | $E_{max}$ = 71.2 ± 1.4 %<br>$IC_{50}$ = 8.85 nM |
| Solabegron | $E_{max}$ = 48.3 ± 3.3 %<br>$IC_{50}$ = 0.14 µM | $E_{max}$ = 63.0* ± 2.7 %<br>$IC_{50}$ = 0.05* µM | $E_{max}$ = 67.1* ± 2.6 %<br>$IC_{50}$ = 0.03* µM | $E_{max}$ = 60.6* ± 2.1 %<br>$IC_{50}$ = 0.09 µM |
| Mirabegron | $E_{max}$ = 71.5 ± 4.9 %<br>$IC_{50}$ = 1.71 µM | $E_{max}$ = 68.2 ± 2.3 %<br>$IC_{50}$ = 0.87* µM | $E_{max}$ = 81.9 ± 3.1 %<br>$IC_{50}$ = 0.33* µM | $E_{max}$ = 68.5 ± 3.2 %<br>$IC_{50}$ = 0.77* µM |

*(*): $p < 0.05$ versus vehicle group*

**FIGURE 8**