SUPPLEMENTARY MATERIALS

Table S1. Treatment outcomes by dose cohort

	Low dose cohort		High dose cohort	
	GMI-1070 N=18	Placebo N=13	GMI-1070 N=25	Placebo N=20
Time to resolution of VOC (composite endpoint)†				
Mean (SD)*	80.79 (59.34)	118.03 (86.77)	131.26 (158.39)	172.47 (170.19)
LS Mean (SE)**	76.69 (31.85)	112.88 (37.12)	131.44 (26.82)	166.06 (30.51)
Median (CI)***	64.8 (37.5, 98.7)	98.0 (47.5, 164.2)	72.4 (44.3, 141.7)	145.5 (45.8, 189.0)
Time to first sustained reduction in VAS pain score				
N	12	12	17	11
Mean (SD)*	49.41 (50.65)	74.59 (78.18)	59.03 (52.46)	80.54 (80.21)
LS Mean (SE)**	46.63 (19.36)	72.38 (19.26)	59.53 (16.08)	79.15 (20.80)
Median (CI)***	73.5 (21.0, 176.9)	67.0 (7.9, 160.5)	72.0 (20.5, 131.8)	179.9 (19.7, 215.5)
Time to sustained decrease in VAS score and transition to oral analgesia				
N	12	12	17	11
Mean (SD)*	69.31 (55.71)	124.57 (85.08)	109.36 (85.36)	152.35 (98.51)
LS Mean (SE) **	65.98 (24.33)	120.01 (24.20)	111.02 (20.21)	152.78 (26.14)
Median (CI)***	80.1 (38.8, 176.9)	140.8 (47.5, 192.6)	135.8 (48.0, 160.3)	215.5 (155.6, 280.7)
Time to agreement about readiness for discharge				
N	18	11	20	17
Mean (SD)*	85.04 (56.97)	133.24 (102.41)	114.42 (95.78)	138.99 (136.64)
LS Mean (SE) **	82.01 (24.36)	134.25 (30.81)	113.22 (22.84)	132.34 (25.69)
Median (CI)***	67.3 (39.6, 105.2)	122.6 (60.0, 279.8)	123.8 (46.3, 162.7)	145.5 (46.7, 196.4)
Time to discharge				
Mean (SD)*	90.36 (59.67)	142.43 (101.55)	149.80 (159.16)	196.62 (173.08)
LS Mean (SE)**	87.96 (33.21)	141.25 (38.71)	150.49 (27.97)	195.38 (31.81)
Median (CI)***	68.1 (44.7, 113.0)	123.6 (60.0, 182.7)	115.5 (59.9, 168.0)	170.5 (53.6, 231.7)
Resolution of VOC				

achieved at various time points N (%)				
48h	7 (38.9)	3 (23.1)	10 (40.0)	5 (25.0)
72h	10 (55.6)	6 (46.2)	12 (48.0)	5 (25.0)
96h	12 (66.7)	6 (46.2)	13 (52.0)	7 (35.0)
120h	14 (77.8)	7(53.8)	14 (56.0)	8 (40.0)
Hospital Length of Stay				
Mean (SD)*	96.76 (59.67)	148.95 (97.97)	158.00 (159.15)	205.47 (172.15)
LS Mean (SE)**	94.64 (33.04)	147.85 (38.51)	158.66 (27.82)	204.47 (31.65)
Median (CI)***	72.9 (51.5, 117.5)	137.6 (66.4, 188.6)	119.1 (66.1, 170.3)	174.1 (70.5, 234.1)
VAS score at discharge				
Mean (SD)*	2.68 (2.97)	3.97 (2.49)	3.27 (2.56)	4.07 (3.24)
Median (range)*	0.8 (0, 9.8)	3.4 (0, 10)	3.2 (0, 9.4)	3.7 (0, 10)
Cumulative parenteral opioid use (MEU mg/kg)				
Mean (SD)*	7.13 (10.84)	29.77 (51.99)	17.27 (25.27)	82.75 (140.02)
LS Mean (SE)**	5.74 (17.18)	26.41 (20.01)	14.32 (14.79)§	76.19 (16.80)
Median (range)*	1.79 (0.7, 7.5)	6.01 (1.7, 12.8)	4.70 (2.4, 18.8)	21.92 (2.9, 130.4)

§ $P < 0.01$
* Descriptive mean or median
** Least squares mean obtained by ANCOVA
***Median obtained by Kaplan-Meier estimate
†Primary endpoint; secondary analysis populations shown

Supplementary Figure 1. GMI-1070-201 enrollment and protocol changes

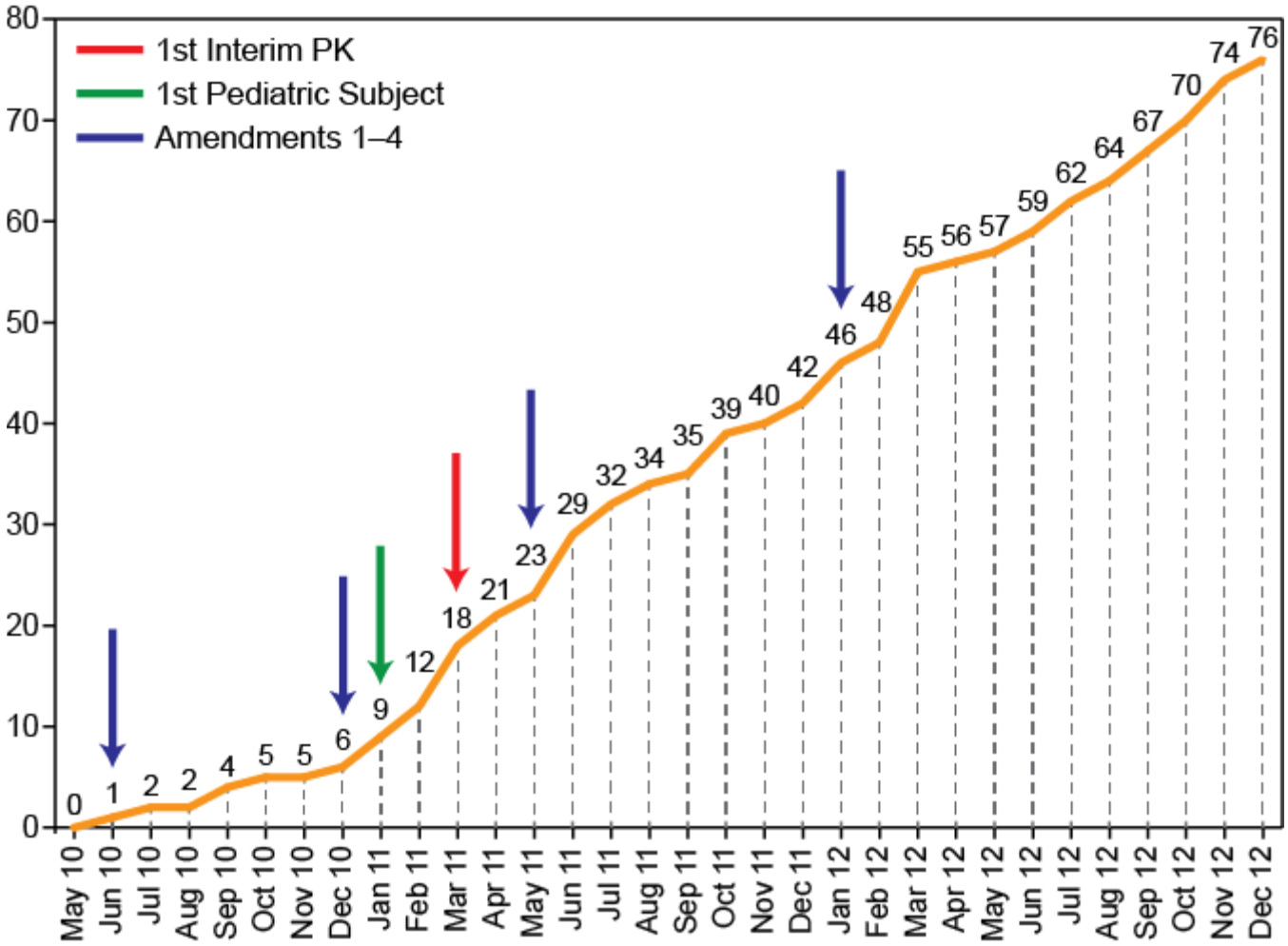

Figure S1. GMI-1070-201 enrollment and protocol changes. Completion of the study required 31 months, from May 2010 to December 2012. The study protocol was amended four times. Amendment 1 extended the age limits to include pediatric subjects age 12-15 years. Amendment 2 extended the upper age limit to 60 years, and loosened limits on recent transfusions and frequency of VOC in the year prior to enrollment. Amendment 3 increased the drug dose to 40 mg/kg loading, then 20 mg/kg Q12H. Amendment 4 extended to 24 hours the window from initial evaluation to treatment and allowed a 48 hour window for outpatient care; it also further loosened the limit on previous transfusions.

Figure S2. Percent of subjects achieving resolution of VOC at various time points

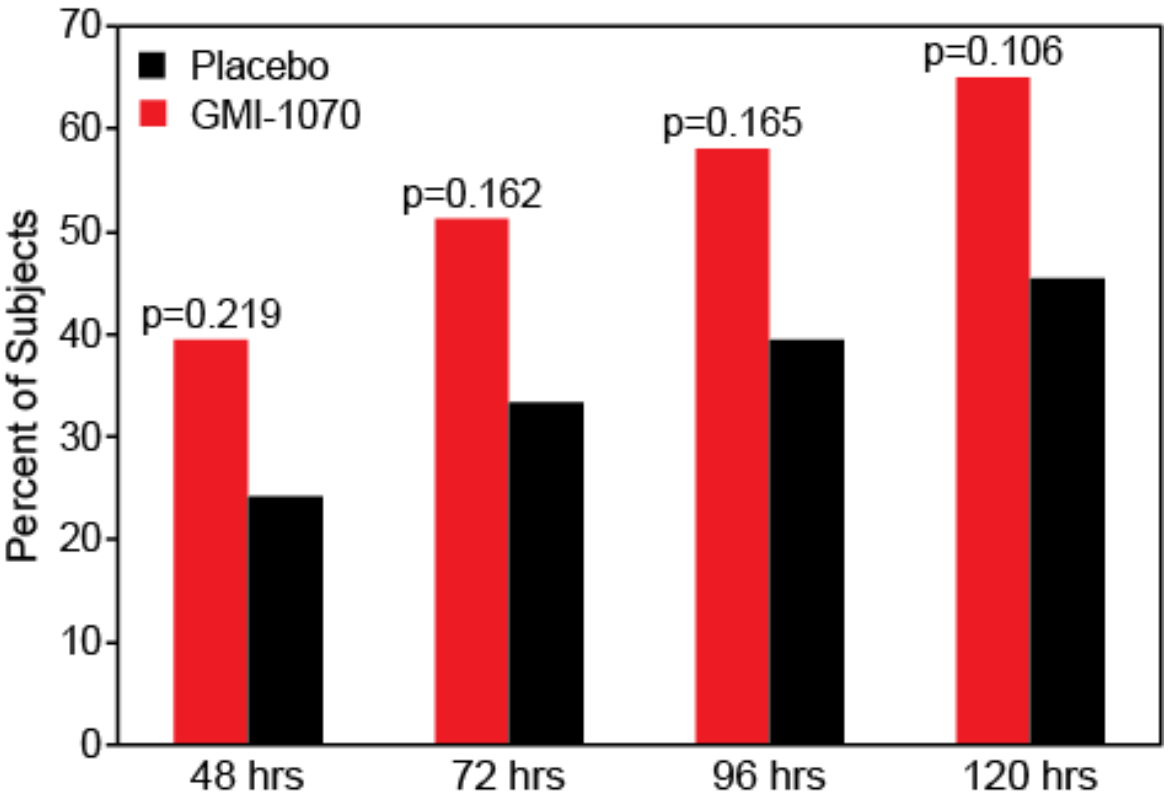

Figure S2. Percent of subjects achieving resolution of VOC at various time points. At every time point from 48 to 120 hours (2 – 5 days), substantially more subjects receiving GMI-1070 had achieved resolution of VOC, compared to those receiving placebo.