Appendix 1 Table M. On-Label Comparative Study Functional Outcomes

Investigator (yr, country, ref #)	Study design	Comparisons No. pts (BMP dose)	Patient diagnosis	Surgical intervention	Outcome measure mean score (p-value)	Outcome measure % improved or success (p-value)	Comment
Boden et al., 2000 USA (71) **Lumbar Spine**	Multicenter, nonblinded RCT	rhBMP2 (4.2-8.4 mg/pt) n=11	single-level lumbar DDD	single-level primary anterior lumbar fusion with interbody fusion cages plus rhBMP2 or ICBG	SF-36 physical function subscale Mean score improvement (points) 3, 6, 12. 24 mos rhBMP2 10, 18, 27, 38	Work status at 24 mos rhBMP2 10 of 11 (91%) pts working	No significant differences between groups
		ICBG n=3			ICBG 13, 27, 37, 37	ICBG 2 of 3 (67%)	
Burkus et al., 2002 USA (72) **Lumbar Spine**	Multicenter, nonblinded RCT	rhBMP2 (4.2-8.4 mg/pt) n=143	single-level lumbar DDD	single-level primary anterior lumbar fusion with interbody fusion cages plus rhBMP2 or ICBG	Median days return to work rhBMP2 64	Neurological status 1.5, 3, 6, 12, 24 mos rhBMP2 80, 84, 78, 82, 83	No significant differences between groups
						Work status 3, 6, 12, 24 mos rhBMP2 38, 51, 55, 66 working	
		ICBG n=136			ICBG 65	Neurological status 1.5, 3, 6, 12, 24 mos ICBG 84, 77, 81, 85, 84	
						Work status 3, 6, 12, 24 mos ICBG 28, 46, 50, 56 working	

Burkus et al., 2003 USA (182) **Lumbar Spine** Note: may include pts in Burkus et al., 2003, (80)	Retrospective combined comparative analysis	rhBMP2 n=277 (dose NR)	single-level lumbar DDD	single-level primary anterior lumbar fusion with interbody fusion cages	SF-36 physical component subscale Mean score improvement (points) pre, 3, 6, 12, 24 mos rhBMP2 9, 12, 14, 16	Work status at 24 mos rhBMP2 103 (75%) who were working presurgery returned to work	rhBMP recipients returned to work a median 55 days sooner than ICBG graft recipients (adjusted p=0.0156)
		ICBG n=402			ICBG 5, 8, 10, 12 (p=0.0015, 0.0004, 0.0003, 0.0007)	ICBG 109 (65%) who were working presurgery returned to work (p NSD)	
Dawson et al., 2009 USA (73) **Lumbar Spine**	Multicenter nonblinded RCT	rhBMP2/CRM n=25 (12 mg/pt)	single-level lumbar DDD	single-level primary instrumented posterolateral lumbar fusion plus rhBMP2 or ICBG	SF-36 physical component subscale Mean score improvement (points) 24 mos rhBMP2/CRM 13	Work status at 24 mos rhBMP2/CRM 8 of 23 (3%5) working	The rhBMP2/CRM group appeared to improve faster than the ICBG group, but this impression was not statistically supported
					SF-36 physical function subscale Mean score improvement (points) 24 mos rhBMP2/CRM 36		
		ICBG n=21			SF-36 physical component subscale Mean score improvement (points) 24 mos ICBG 10	ICBG 6 of 20 (30%) working	

					SF-36 physical function subscale Mean score improvement (points) 24 mos ICBG 18		
Govender et al. for the BESTT study group 2002 South Africa (74) **Open Tibial Fractures**	Multi-center, single blind, RCT	rhBMP2 (1) n=151 (6 mg/patient) rhBMP2 (2) n=149 (12 mg/patient) (3) n=150 Standard care (IM nail fixation and soft tissue management)	Open tibial fracture where the major component was diaphyseal	IM nail fixation and soft tissue management	NR	NR	
Swiontkowski et al., 2006 USA (81) **Open Tibial Fractures** Note: This paper reports	Subgroup analysis of combined data from two prospective randomized trials with identical designs	rhBMP2 (1) n=169 (12 mg/patient)	Acute open tibial fracture	IM nail fixation and soft tissue management	NR	NR	

on 131 of the same patients included in Govender et al., 2002 (74)		(2) n=169 Standard care (IM nail fixation and soft tissue management)					
Boyne et al., 2005 USA (75) **Maxillofacial and Dental**	Multicenter randomized dose-comparison, safety and efficacy study	rhBMP2/ACS (6-24 mg/pt) n=18	< 6 mm alveolar bone height in the posterior maxilla	staged bilateral or unilateral maxillary sinus floor augmentation	NR	Prosthesis implantation into newly induced bone rhBMP2/ACS 0.75 mg/mL 83 Successful prosthetic functional loading at 36 mos. (% patients) rhBMP2/ACS 0.75 mg/mL 100/67 (12 of 12 observed/12 of 18 enrolled) Bone quality at dental implant placement (Branemark criteria) I, >I-II, >II-III, >III-IV (%) rhBMP7/ACS 0.75 mg/mL (n=15) 0, 7, 53, 40	Patient success was defined as having an augmentation procedure with at least one implant placed into newly formed bone without additional augmentation, achieved osseointegration of sufficient number of implants to allow prosthetic device implant, and maintained prosthetic use for 36 mos. following functional loading

		rhBMP2/ACS (15-48 mg/pt) n=17				Prosthesis implantation into newly induced bone rhBMP2/ACS 1.50 mg/mL 88	
						Successful prosthetic functional loading at 36 mos. (% patients) rhBMP2/ACS 1.50 mg/mL 100/76 (13 of 13 observed/13 of 17 enrolled)	
						Bone quality at dental implant placement (Branemark criteria) I, >I-II, >II-III, >III-IV (%) rhBMP7/ACS 1.50 mg/mL (n=15) 0, 20, 60, 20	
		AGB n=13				Prosthesis implantation into newly induced bone rhBMP2/ACS AGB 100	

						Successful prosthetic functional loading at 36 mos. (% patients) AGB 100/62 (8 of 8 observed/8 of 13 enrolled)	
						Bone quality at dental implant placement (Branemark criteria) I, >I-II, >II-III, >III-IV (%) rhBMP7/ACS AGB (n=12) 0, 8, 58, 33	
Fiorellini et al., 2005 USA (76) **Maxillofacial and Dental**	Double-blind, multicenter randomized, placebo-control dose-comparison, safety and efficacy study	rhBMP2/ACS (mn dose 0.9 mg/pt) n=22	≥ 50% buccal bone loss of the extraction socket(s)	extraction socket augmentation	NR	Dental implant placement without secondary augmentation rhBMP2/ACS 0.75 mg/mL 55	
		rhBMP2/ACS (mn dose 1.9 mg/pt) n=21				1.50 mg/mL 86	
		Placebo n=17				Placebo 59	
		No Tx n=20				No tx 45 (p=0.009 vs no tx)	

Triplett et al., 2009 USA (77) **Maxillofacial and Dental**	Multicenter, nonblinded RCT	rhBMP2/ACS n=80 (12-24 mg/pt)	< 6 mm alveolar bone height in the posterior maxilla	staged bilateral or unilateral maxillary sinus floor augmentation	NR	Prosthesis implantation into newly induced bone rhBMP2/ACS 82	Patient success was defined as having an augmentation procedure with at least one implant placed into newly formed bone without additional augmentation, achieved osseointegration of sufficient number of implants to allow prosthetic device implant, and maintained prosthetic use for 24 mos. following functional loading
						Successful prosthetic functional loading at 24 mos. (% patients) rhBMP2/ACS 76	
		AGB n=80				Prosthesis implantation into newly induced bone AGB 95	
						Successful prosthetic functional loading at 24 mos. (% patients) AGB 91 (p=0.0166)	
van den Bergh et al., 2000 Netherlands (82)	Retrospective cohort study	rhBMP7/ACS n=3 (2.5 mg/pt)	partly edentulous	maxillary sinus floor augmentation	NR	Implant placement at 6 mos rhBMP7/ACS 33	Statistical analysis not done, too few observations

Maxillofacial and Dental		ICBG n=3				ICBG 100	
Calori et al., 2008 Italy (78) **Long Bone Nonunion**	Single-center, nonblinded RCT	rhBMP7/ACS n=60 (3.5-7.0 mg/pt) PRP n=60	post-traumatic atrophic nonunion for ≥ 9 mos, with no signs of healing over the last 3 mos	open reduction internal fixation (ORIF), external fixation (EF), or reamed intramedullary nailing (IM) with rhBMP7 or PRP	NR	NR	
Dahabreh et al., 2008 (83) **Long Bone Nonunion**	Retrospective cohort study	rhBMP7/ACS n=15 (3.5 mg/pt) ICBG n=12	tibial fracture nonunion with clinical and radiographic failure to progress to union for ≥ 9 mos. following initial fracture stabilization	open reduction internal fixation (ORIF), exchange intramedullary nailing (IM), or Ilizarov, with rhBMP7 or ICBG	NR	NR	

Friedlaender et al., 2001 (79) **Long Bone Nonunion**	Multicenter, partially blinded RCT	rhBMP7/ACS n=61 (3.5-7.0 mg/pt)	tibial nonunion for ≥ 9 mos, with no signs of healing over the last 3 mos	IM rod fixation with rhBMP7/ACS or AGB	NR	Weight-bearing 9 mos rhBMP7/ACS 86	
		AGB n=61				AGB 85	