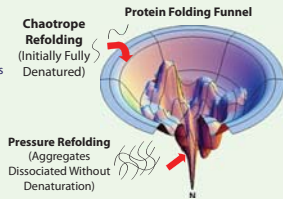


PreEMT™ Technology: An "Elegant Method"



- Purely thermodynamics
- High hydrostatic pressure disaggregates and properly refolds proteins
- Enables proprietary products with enhanced safety
- Scalable technology with broad applications

BaroFeron™

- Recombinant human interferon beta-1b for subcutaneous injection
- Manufactured from E. coli using PreEMT Technology
- Essentially free of protein aggregates in final formulation
- Formulated without human serum albumin

Methods

- Single dose pharmacokinetics were assessed in Spague-Dawley Rats (naïve), cynomolgus monkeys (non-naïve), and rhesus monkeys (non-naïve)
- Serum levels of rhIFN beta-1b were measured with an ELISA method
- Neopterin levels were measured with a commercial kit qualified for use on monkey samples
- Animal studies were conducted by Charles Rivers Laboratories (in-life) with IUCAC approval
- Samples were analyzed by Prevalere Life Sciences

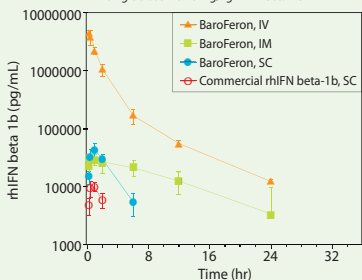
Spague Dawley Rats Treatment Groups (n = 4 males/group)

Group #	Treatment				Route
	Test Article	Dose (mg/kg)	Conc. (mg/mL)	Dose Vol. (mL/kg)	
1 (♂)	BaroFeron	0.2	0.10	2.0	Intravenous (IV)
2 (♂)	BaroFeron	0.2	0.10	2.0	Intramuscular (IM)
3 (♂)	BaroFeron	0.2	0.10	2.0	Subcutaneous (SC)
4 (♂)	Commercial rhIFN beta-1b	0.2	0.10	2.0	Subcutaneous (SC)

Plasma samples obtained pre-dose, 15 and 30 minutes, and 1, 2, 6, 12 and 24 hr post-dose for all groups, and 36 hr post-dose for Groups 3 and 4.

Pharmacokinetics - Rats

Single Dose = 0.20 mg/kg rhIFN beta-1b



BaroFeron™, an Interferon Beta Product with Improved Bioavailability

J. L. Cleland, M. Rosendahl, S. P. Eisenberg, M. Seefeldt, D. Haughey
BaroFold Inc., Boulder, CO | Prevalere Life Sciences, Whitesboro, NY 13492

Pharmacokinetic Parameters for rhIFN beta-1b in Sprague Dawley Rats

Group	C _{max} (pg/mL)	T _{max} (hr)	AUC _{0-n} (hr*pg/mL)	AUC _{0-∞} (hr*pg/mL)	t _{1/2} (hr)
1 (♂) (BaroFeron, IV)	4617883 ± 675033	0.31 ± 0.13	9461435 ± 2238495	9574428 ± 2238495	3.42 ± 1.74
2 (♂) (BaroFeron, IM)	31623 ± 5374.7	0.99 ± 0.69	295937 ± 159848	444057 ± 188354	9.71 ± 3.76
3 (♂) (BaroFeron, SC)	43225 ± 11293	0.99 ± 0.02	134592 ± 29014	148377 ± 31608	1.70 ± 0.365
4 (♂) (Commercial rhIFN beta-1b SC)	10469 ± 2186	0.75 ± 0.26	14263 ± 1189	41526 ± 27074	2.84 ± 2.73

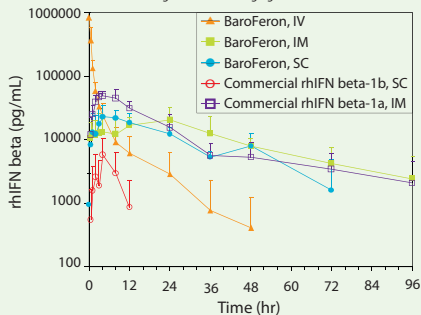
Non-naïve cynomolgus monkey treatment groups (n = 4 /group)

Group #	Test Article	Treatment			Route
		Dose (mg/kg)	Conc. (mg/mL)	Dose Vol. (mL/kg)	
1	BaroFeron	0.05	0.25	0.20	Intravenous (IV)
2	BaroFeron	0.05	0.25	0.20	Intramuscular (IM)
3	BaroFeron	0.05	0.25	0.20	Subcutaneous (SC)
4	Commercial rhIFN beta-1b	0.05	0.25	0.20	Subcutaneous (SC)
5	Commercial rhIFN beta-1a	0.05	0.06	0.83	Intramuscular (IM)

Plasma samples were taken pre-dose, 5 (IV only) and 30 min, 1, 2, 3, 4, 8, 12, 24, 36, 48, 72 and 96hr post-dose.

Pharmacokinetics - Cynomolgus Monkeys

Single Dose = 0.05 mg/kg rhIFN beta

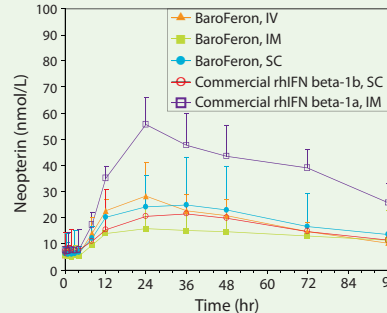


Pharmacokinetic Parameters for rhIFN beta in Cynomolgus Monkeys*

Group	C _{max} (pg/mL)	T _{max} (hr)	AUC _{0-n} (hr*pg/mL)	AUC _{0-∞} (hr*pg/mL)	t _{1/2} (hr)
1 (BaroFeron, IV)	846554 ± 145275	0.09 ± 0.00	768153 ± 254292	819438 ± 276783	8.13
2 (BaroFeron, IM)	22741 ± 13216	17.77 ± 11.18	913784 ± 524483	1092001 ± 557025	34.56 ± 12.62
3 (BaroFeron, SC)	24219 ± 10585	5.94 ± 2.29	605319 ± 258834	860693 ± 349484	25.55 ± 12.50
4 (Commercial rhIFN beta-1b SC)	6163 ± 4216	4.46 ± 2.42	43991 ± 8232	62052 ± 9908	5.02 ± 4.78
5 (Commercial rhIFN beta-1a SC)	49881 ± 12774	4.98 ± 1.90	1117557 ± 446674	1215595 ± 504652	18.79 ± 9.98

* n = 4 monkeys per group for BaroFeron, IV, IM and SC and Commercial rhIFN beta-1a, IM; n = 2 monkeys for Commercial rhIFN beta-1b, SC as a result of 2 monkeys with plasma levels below the lower limit of quantitation.

Pharmacodynamics - Cynomolgus Monkeys

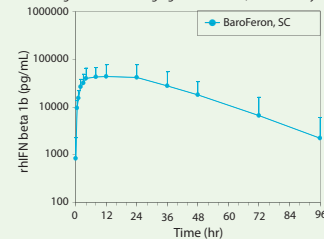


Plasma Neopterin Exposure Parameters in Cynomolgus Monkeys after rhIFN beta administration

Group	C _{max} (nmol/L)	T _{max} (hr)	AUC _{0-n} (hr*nmol/L)
1 (BaroFeron, IV)	24.01 ± 5.02	26.60 ± 14.86	1201 ± 231
2 (BaroFeron, IM)	11.74 ± 3.76	51.28 ± 40.13	727 ± 291
3 (BaroFeron, SC)	19.31 ± 5.89	35.73 ± 9.85	1210 ± 419
4 (Commercial rhIFN beta-1b SC)	15.12 ± 2.97	35.70 ± 9.89	879 ± 200
5 (Commercial rhIFN beta-1a IM)	50.42 ± 11.03	26.33 ± 6.45	2924 ± 650

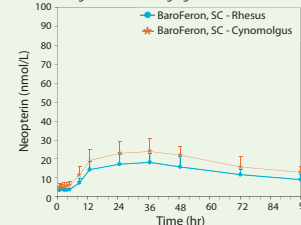
Pharmacokinetics - Rhesus Monkeys

Single Dose = 0.05 mg/kg rhIFN beta-1b; n = 4 monkeys



Pharmacodynamics - Monkeys

Single Dose = 0.05 mg/kg rhIFN beta-1b



Summary

- BaroFeron was well tolerated (i.e., no clinical signs noted) following single IV, IM, and SC administration
- Expected pharmacodynamic responses were achieved following the administration of BaroFeron in monkeys
- The SC bioavailability of rhIFN beta-1b in BaroFeron was 4 fold and 10 fold higher than Commercial rhIFN beta-1b in rats and cynomolgus monkeys, respectively
- The increase in bioavailability for BaroFeron could be related to differences in formulation (HSA) and/or reduced aggregation
- The IM bioavailability of rhIFN beta-1b in BaroFeron was comparable to the IM bioavailability of Commercial rhIFN beta-1a

Conclusions

- BaroFeron, a novel 'aggregate-free' preparation of rhIFN beta-1b, has greater bioavailability administered SC than commercial product.
- The greater SC bioavailability and longer elimination half-life of rhIFN beta-1b in BaroFeron as compared to commercial product may lead to:
 - Less frequent administration of BaroFeron
 - Potential for equal or greater efficacy at lower rhIFN beta-1b dose of BaroFeron
- The lack of aggregates in BaroFeron may result in reduced immunogenicity compared to the commercial product.