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Confidential information

Pilot Clinical Study of Dietary Supplement, Young Bones™ (A Traditional Chinese Herbal Formula) For Improvement of Aging, including Bone Mineral Loss, Pain, Mobility And Nocturnal Polyuria in Women

Final 12-Week Report

12/1/2003

Introduction

March 2003 the Osteoporosis Education Project began a clinical pilot study of the traditional Chinese herbal formula known as Young Bones™. The aim of this clinical trial was to assess the effect of this herbal formula on aging/menopause symptoms including bone mineral loss, pain, mobility problems and excessive nighttime urination in postmenopausal women.

This 12 week pilot study had two endpoints: (a) changes in bone resorption at 6 and 12 weeks, and; (b) changes in aging/menopausal symptoms at 12 weeks.

Bone resorption was assessed with the Ostex International serum N-telopeptide assay (Serum NTx). The "least significant change" for this assay is 14% at a confidence interval of 90%. The symptoms were assessed via a questionnaire developed by Sagittarius Life Science, Corp.

By the end of June, 2003 the last subjects were successfully screened and incorporated into the study. By the end September the last serum samples of this 12 weeks study were collected. The final 12-week symptom questionnaires were also administered at this time.

The study in its entirety included 14 regular subjects, plus two extra, grouped as follows:

- A Later Post-Menopause Group
  This group involved women more than five years past menopause.

Eight subjects were in this group. The subjects ranged in age from 47 to 64.

- The Early Post-Menopause Group
  This group involves women five or less years past menopause.
  Six subjects were in this group. These ranged in age from 51 to 62.

- Two extra subjects.

  One subject (J. Hunt), age 65, did not qualify for the study because her serum NTX was low, yet she has many symptoms which should benefit from Young Bones™ use. She used Young Bones™ and was assessed only for changes in symptoms at 6 and 12 weeks.

  The other subject (J. Bender) is a 54-year-old perimenopause woman (Susan's secretary) who wanted to use the herbs to help with her menopause symptoms. She used Young Bones™ and was assessed only for changes in symptoms at 6 and 12 weeks.

Reports Submitted to Date

In late August, Dr. Susan Brown submitted a Six Month Report. On October 6th she forwarded the tabulation of the symptom changes at 12 weeks use of Young Bones™. Copies of the baseline and 12-week symptom questionnaires were also sent to Dr. Liu at this time.

This Current Report

This current and final report consists of four sections.

- The first section reports on the change in bone resorption with 6, and then 12, weeks Young Bones™ use.
- The second section summarizes the changes in aging/menopausal symptoms with 12 weeks use of Young Bones™.
- The third section considers the issue of product adverse effects.
- The fourth section provides the blood chemistries available to date on the two original study subjects who also had markers of bone formation and BMD tests.

Section # 1 Young Bones™ and Bone Resorption Changes

In this twelve-week pilot study the rate of bone resorption was measured using the Ostex International serum NTx test. Serum NTx levels were tested at baseline, 6 weeks and 12 weeks.

Serum NTx at Baseline

At baseline all 14 subjects had serum NTx scores above the premenopausal mean of 12.6. The total group average serum NTx was15.36 with a range of 12.70 to 18.70. Table #1 lists the baseline serum NTx scores for all 14 subjects.

Table #2 displays the individual NTx baseline scores; the group averages and ranges sfor the Subjects #1 through #8 who comprised the "Later Menopause Group". These women were more than five years past their last period".

Table #3 details the same data for subjects # 9 through #14 who comprised the "Early Menopause Group". These women were five or less years since their last period.

As is obvious both groups had mean baseline NTx scores well above the premenopausal mean of 12.6. On the average the Early Menopause Group had higher NTx bone resorption scores than the Later Menopause Group.

Table 1

Baseline Serum NTx Scores
All Study Subjects

		Baseline NTx Serum Score
1	MH	16.80
2	GDD	16.00
3	KB	15.70
4	KC	13.40
5	CP	14.00
6	JB	19.00
7	VS	15.30
8	SB	12.70
9	BM	13.70
10	MS	16.00
11	BL	16.00
12	CVM	16.20
13	NC	16.20
14	DB	18.70
	Average	15.69
	Range	12.7 to 19.0

Later Menopause Group
More than 5 Years Past Last Period

Early Menopause Group
Less Than 5 Years Since Last Period

Table 2
Later Menopause Group
Baseline NTx Score

		Baseline NTx Serum Score
1	MH	16.8
2	GDD	16.0
3	KB	15.7
4	KC	13.4
5	CP	14.0
6	JB	19.0
7	VS	15.3
8	SB	12.7
	Average	15.4
	Range	12.7 to 19.0

Table 3
Early Menopause Group
Baseline NTx Score

		Baseline NTx Serum Score
1	BM	13.70
2	MS	16.00
3	BL	16.00
4	CVM	16.20
5	NC	16.20
6	DB	18.70
	Average	16.13
	Range	13.7 to 18.7

Serum NTx At Six Weeks

At the six week point there was a near uniform increase in the serum NTx levels. In only two subjects (14%) did we fail to find reported an increase in serum NTx at six weeks. Of these two, one subject was virtually stable with an insignificant –0.53 decease in NTx (subject#14); and, another subject, #7, experienced a significant –19.61% decrease in serum NTx. Table #4 compares the NTx scores at baseline and six weeks.

The total group average increase in NTx at six weeks was 20.22%. As displayed in Tables #5 and #6, the Later Menopause Group had a significantly greater increase in NTx at six weeks than did the Early Menopause Group.

Table 4

Serum NTx Changes Baseline to Six Weeks
All Study Subjects

		Baseline NTx Serum Score	6 Week NTx Score	% NTx Change Baseline to 6 Wks
1	MH	16.80	19.90	18.45%
2	GDD	16.00	23.40	46.25%
3	KB	15.70	17.30	10.19%
4	KC	13.40	25.70	91.79%
5	CP	14.00	19.20	37.14%
6	JB	19.00	20.00	5.26%
7	VS	15.30	12.30	-19.61%
8	SB	12.70	12.90	1.57%
9	BM	13.70	16.00	16.79%
10	MS	16.00	21.00	31.25%
11	BL	16.00	19.10	19.38%
12	CVM	16.20	NA	NA
13	NC	16.20	17.00	4.94%
14	DB	18.70	18.60	-0.53%
		Average Percent Change		20.22%
		Range of Percent Change		91.79% to -19.61%

	Later Menopause Group More than 5 Years Past Last Period
	Early Menopause Group Less Than 5 Years Since Last Period

Table 5
Serum NTx Changes Baseline to 6 Weeks: Later Menopause Group

		Baseline NTx Serum Score	6 Week NTx Score	% NTx Change Baseline to 6 Wks
1	MH	16.80	19.90	18.45%
2	GDD	16.00	23.40	46.25%
3	KB	15.70	17.30	10.19%
4	KC	13.40	25.70	91.79%
5	CP	14.00	19.20	37.14%
6	JB	19.00	20.00	5.26%
7	VS	15.30	12.30	-19.61%
8	SB	12.70	12.90	1.57%
		Average Percent Change		23.88%
		Range of Percent Change		91.79% to -19.61%

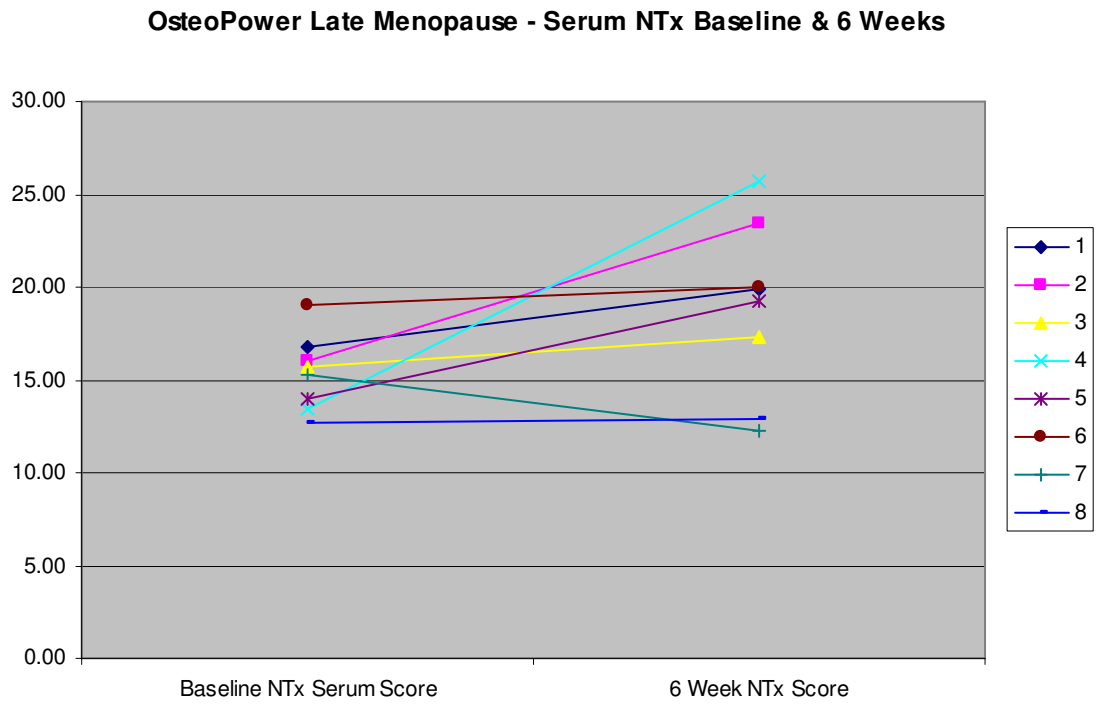
Table 6
Serum NTx Changes Baseline to 6 Weeks: Early Menopause Group

		Baseline NTx Serum Score	6 Week NTx Score	% NTx Change Baseline to 6 Wks
1	BM	13.70	16.00	16.79%
2	MS	16.00	21.00	31.25%
3	BL	16.00	19.10	19.38%
4	CVM	16.20	Data Unavailable**	NA
5	NC	16.20	17.00	4.94%
6	DB	18.70	18.60	-0.53%
		Average Percent Change		14.36%
		Range of Percent Change		31.25% to -0.53%

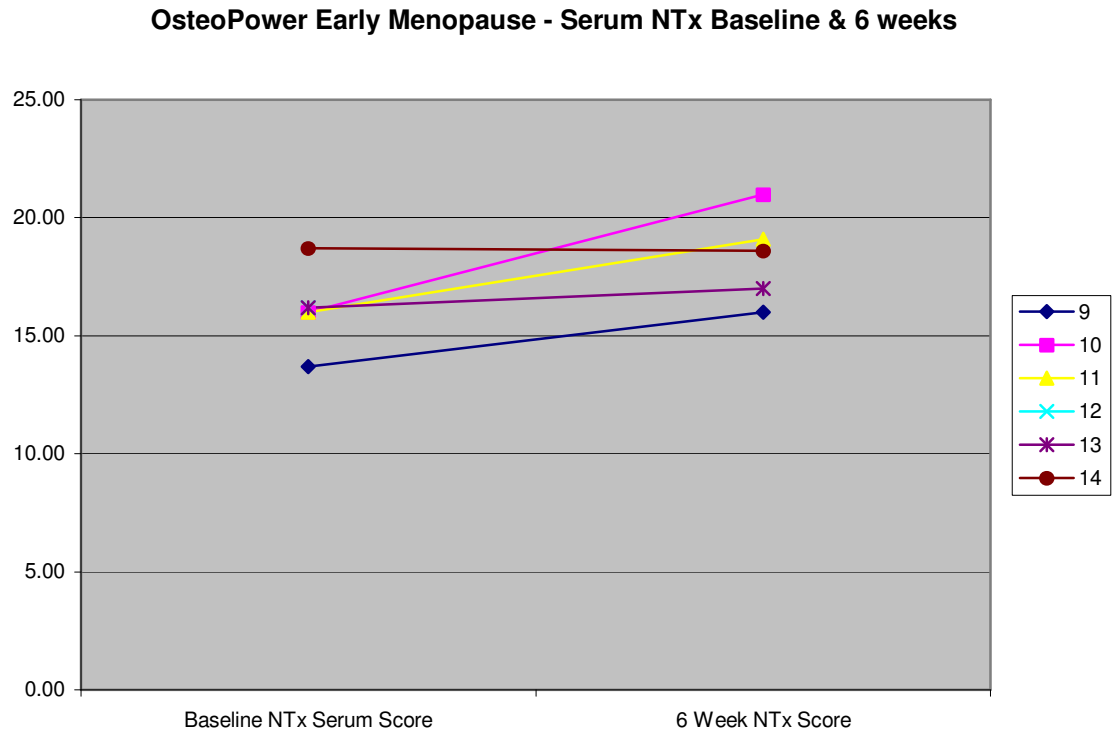
**For subject CVM in the early menopause group the 6-week serum sample was damaged and exhausted by the testing laboratory.

Graphs #1 and #2 illustrate these changes in NTx from baseline to six weeks. Graph #1 depicts the Later Menopause Group (more than 5 years since last period). Graph #2 depicts the Early Menopause Group (5 or less years since last period)

Graph 1



Graph 2



Change in Serum NTx From 6 Weeks to 12 Weeks

Of the total 14 subjects, 10 (71%) experienced a reduction in NTx between 6 weeks and 12 weeks. Of these the reduction was 14% or greater, and thus statistically significant, for seven subjects (50% of all subjects).

Three subjects (21%) experienced an increase in NTx from 6 to 12 weeks. Two of these subjects had significant increase and one an insignificant increase. For one subject, #12 CVM, there is no calculation of change in serum NTx from 6 weeks to 12 weeks because her serum sample was damaged and exhausted in the testing laboratory.

Table #7 lists the changes in NTx from 6 weeks to 12 weeks for all study subjects.

Table 7

Serum NTx Change From 6 Weeks to 12 Weeks
All Study Subjects

		6 week NTx Score	12 week NTx Score	% NTx Change 6 to 12 weeks
1	MH	19.90	13.30	-33.17%
2	GDD	23.40	9.50	-59.40%
3	KB	17.30	13.40	-22.54%
4	KC	25.70	12.60	-50.97%
5	CP	19.20	16.80	-12.50%
6	JB	20.00	23.30	16.50%
7	VS	12.30	17.10	39.02%
8	SB	12.90	9.50	-26.36%
9	BM	16.00	14.80	-7.50%
10	MS	21.00	10.90	-48.10%
11	BL	19.10	13.80	-27.75%
12	CVM	Data Unavailable**	16.00	NA
13	NC	17.00	18.80	10.59%
14	DB	18.60	18.20	-2.15%
			Average Percent Change	-18.51%
			Range of Percent Change	39.02% to -59.4%

Later Menopause Group More than 5 Years Past Last Period
Early Menopause Group Less Than 5 Years Since Last Period

**For subject CVM in the early menopause group the 6-week serum sample was damaged and exhausted by the testing laboratory.

Tables #8 and 9 detail the change in serum NTx from 6 weeks to 12 weeks by subgroup.

Table 8 Later Menopause Group

		6 week NTx Score	12 week NTx Score	% NTx Change Baseline to 12 weeks
1	MH	19.90	13.30	-33.17%
2	GDD	23.40	9.50	-59.40%
3	KB	17.30	13.40	-22.54%
4	KC	25.70	12.60	-50.97%
5	CP	19.20	16.80	-12.50%
6	JB	20.00	23.30	16.50%
7	VS	12.30	17.10	39.02%
8	SB	12.90	9.50	-26.36%
			Average	-18.68%
			Range	39.02% to -59.40%

Table 9 Early Menopause Group

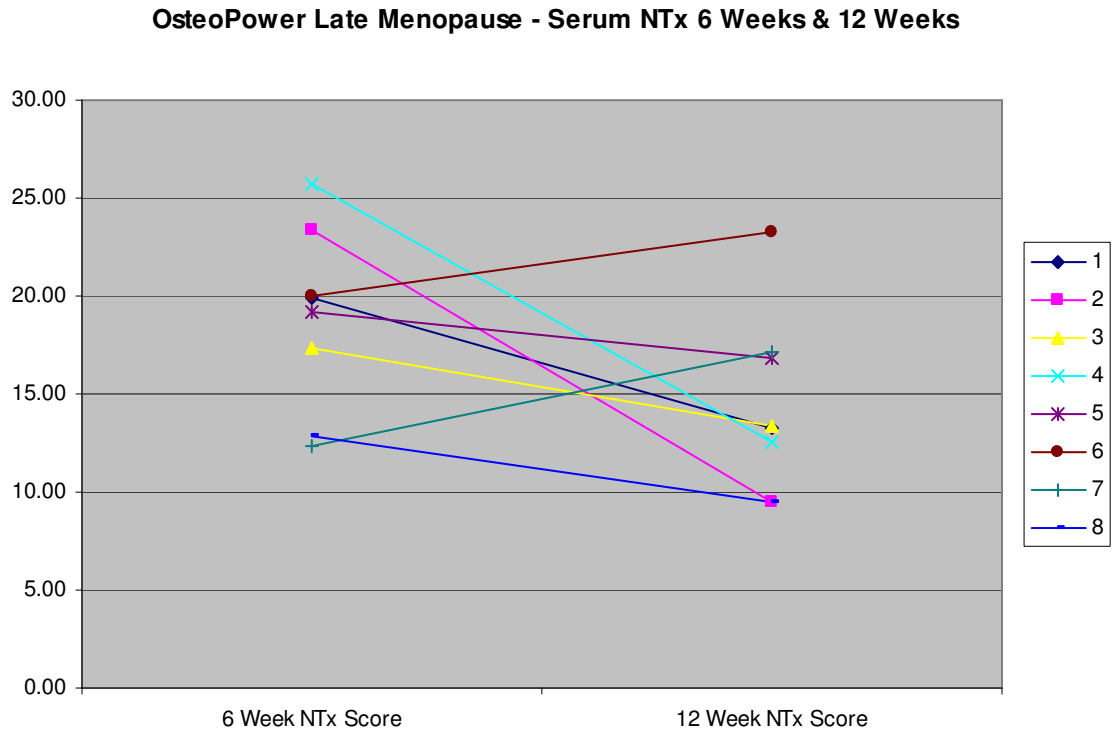
	6 week NTx Score	12 week NTx Score	% NTx Change Baseline to 12 weeks
BM	16.00	14.80	-7.50%
MS	21.00	10.90	-48.10%
BL	19.10	13.80	-27.75%
CVM	Data Unavailable**	16.00	NA
NC	17.00	18.80	10.59%
DB	18.60	18.20	-2.15%
		Average	-14.98%
		Range	10.59% to -48.10%

**For subject CVM in the early menopause group the 6-week serum sample was damaged and exhausted by the testing laboratory.

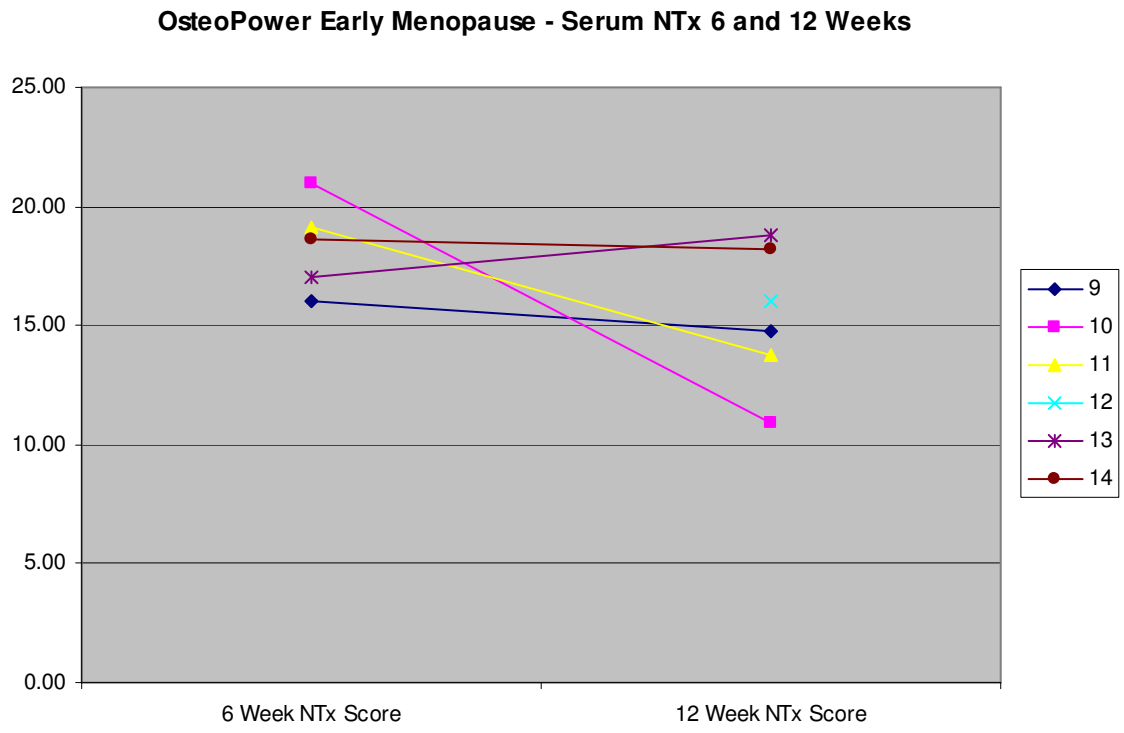
Just as the Later Menopause Group experienced a greater increase in bone resorption from baseline to six weeks, this group also had a greater decrease in NTx from 6 weeks to 12 weeks.

Graph # 3 illustrates the bone resorption change from 6 weeks to 12 weeks in the Later Menopause Group. Graph #4 illustrates changes in the Early Menopause Group.

Graph 3



Graph 4



Change From Baseline to 12 Weeks

At the twelve-week point ten of the total fourteen study subjects, that is 71% of the total subjects, experienced a reduction in NTx from baseline. In six subjects (43%) this reduction was greater than 14% and thus statistically significant. The other four subjects had increases in NTx from baseline to 12 weeks, of these two were significant and two did not reach significance. Table 10 presents the 12-week data for all study participants.

Table # 11 presents the data on NTx serum changes from baseline to 12 weeks for the Later Menopause Group. Table #12 gives this information for the Early Menopause Group. Graph #5 illustrates the changes in serum NTx between baseline and 12 weeks among the Later Menopause Group and Graph #6 illustrates the same for the Early Menopause Group.

Table 10 Change in Serum NTx Baseline to 12 Weeks
All Study Subjects

		Baseline NTx Serum Score	12 week NTx Score	% NTx Change Baseline to 12 weeks
1	MH	16.80	13.30	-20.83%
2	GDD	16.00	9.50	-40.63%
3	KB	15.70	13.40	-14.65%
4	KC	13.40	12.60	-5.97%
5	CP	14.00	16.80	20.00%
6	JB	19.00	23.30	22.63%
7	VS	15.30	17.1	11.76%
8	SB	12.70	9.50	-25.20%
9	BM	13.70	14.80	8.03%
10	MS	16.00	10.90	-31.88%
11	BL	16.00	13.80	-13.75%
12	CVM	16.20	16.00	-1.23%
13	NC	16.20	18.80	16.05%
14	DB	18.70	18.20	-2.67%
		Average Percent Change		-5.82%
		Range of Percent Change		22.63% to -40.63%

	Later Menopause Group More than 5 Years Past Last Period
	Early Menopause Group Less Than 5 Years Since Last Period

Table 11

Late Menopause Group

		Baseline NTx Serum Score	12 week NTx Score	% NTx Change Baseline to 12 weeks
1	MH	16.80	13.30	-20.83%
2	GDD	16.00	9.50	-40.63%
3	KB	15.70	13.40	-14.65%
4	KC	13.40	12.60	-5.97%
5	CP	14.00	16.80	20.00%
6	JB	19.00	23.30	22.63%
7	VS	15.30	17.1	11.76%
8	SB	12.70	9.50	-25.20%
		Average Percent Change		-6.61%
		Range of Percent Change		22.63% to – 40.63

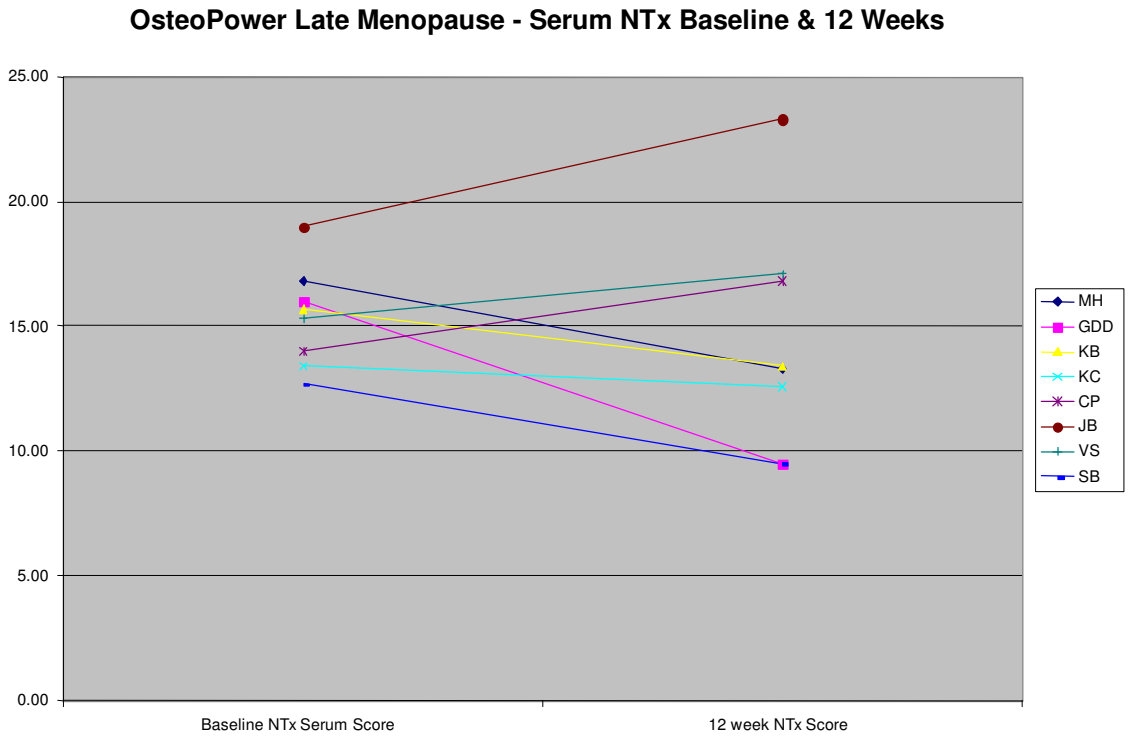
Table 12

Early Menopause Group

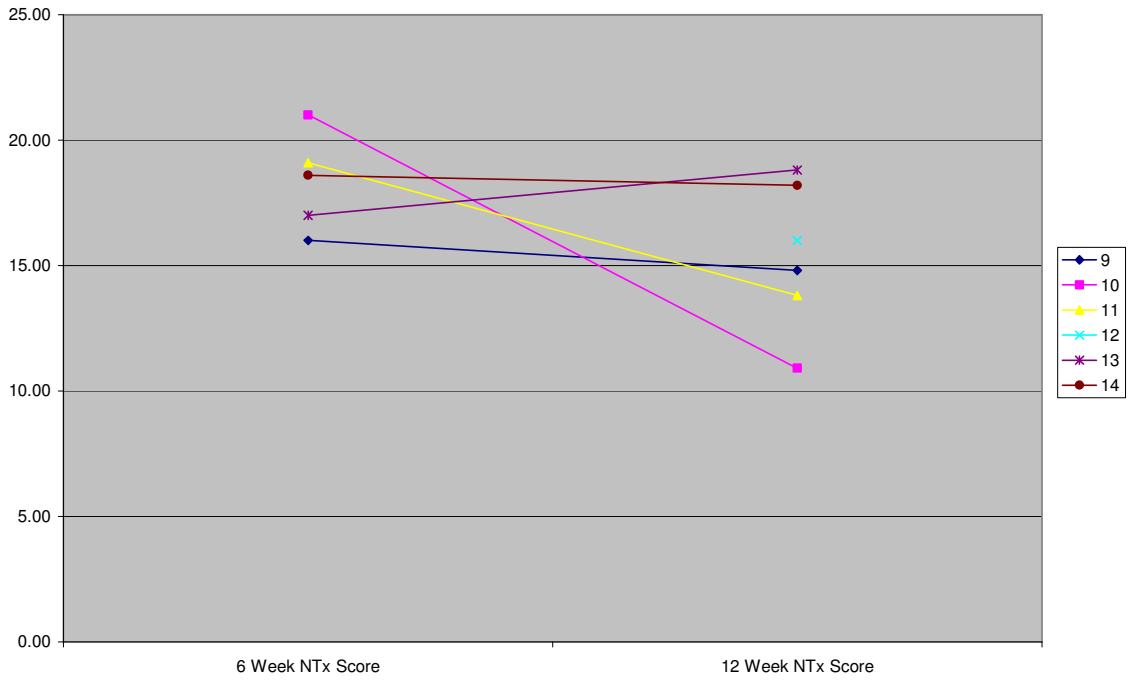
		Baseline NTx Serum Score	12 week NTx Score	% NTx Change Baseline to 12 weeks
1	BM	13.70	14.80	8.03%
2	MS	16.00	10.90	-31.88%
3	BL	16.00	13.80	-13.75%
4	CVM	16.20	16.00	-1.23%
5	NC	16.20	18.80	16.05%
6	DB	18.70	18.20	-2.67%
		Average Percent Change		-4.24%
		Range of Percent Change		16.05% to -31.88%

At 12 weeks the Later Menopause Group showed a one-third greater reduction in serum NTX as than the Early Menopause Group. Graph #5 and Graph #6 display this NTx data by subgroup.

Graph 5



Graph 6



As a summary reference table, Table # 13 lists all three NTx scores for all fourteen-study participants. Tables # 14 and #15 detail this data for the two subject groups separately.

Table 13 NTx Data: All Study Subjects

	Osteo Power	Baseline NTx Serum Score	6 week NTx Score	12 week NTx Score
1	MH	16.80	19.90	13.30
2	GDD	16.00	23.40	9.50
3	KB	15.70	17.30	13.40
4	KC	13.40	25.70	12.60
5	CP	14.00	19.20	16.80
6	JB	19.00	20.00	23.30
7	VS	15.30	12.30	17.1
8	SB	12.70	12.90	9.50
9	BM	13.70	16.00	14.80
10	MS	16.00	21.00	10.90
11	BL	16.00	19.10	13.80
12	CVM	16.20	NA	16.00
13	NC	16.20	17.00	18.80
14	DB	18.70	18.60	18.20
	Average	15.46	18.65	14.60
	Range	12.7 to 19.0	12.3 to 25.7	9.5 to 23.3

Later Menopause Group
More than 5 Years Past Last Period
Early Menopause Group
Less Than 5 Years Since Last Period

Table 14
Total NTx Data
Later Menopause Group

	Osteo Power	Baseline NTx Serum Score	6 week NTx Score	12 week NTx Score
1	MH	16.80	19.90	13.30
2	GDD	16.00	23.40	9.50
3	KB	15.70	17.30	13.40
4	KC	13.40	25.70	12.60
5	CP	14.00	19.20	16.80
6	JB	19.00	20.00	23.30
7	VS	15.30	12.30	17.1
8	SB	12.70	12.90	9.50
	Ave.	15.36	18.84	14.44
	Range	12.7 to 19.0	12.3 to 25.7	9.5 to 23.3

Table 15
Total NTx Data
Early Menopause Group

	Osteo Power	Baseline NTx Serum Score	6 week NTx Score	12 week NTx Score
1	BM	13.7	16.0	14.8
2	MS	16.0	21.0	10.9
3	BL	16.0	19.1	13.8
4	CVM	16.2	NA	16.0
5	NC	16.2	17.0	18.8
6	DB	18.7	18.6	18.2
	Average	16.13	18.34	15.42
	Range	13.7 to 18.7	16.0 to 21.0	13.8 to 18.8

Section # 2 Overview of Aging/Menopause Symptom Changes

Symptom changes were measured using a standardized questionnaire developed by Sagitarrius Life Science Corp. On October 6th we forwarded to Dr. Liu the completed baseline and 12-week symptoms questionnaires and our full data tabulation.

The questionnaire was quite lengthy and assessed many symptoms. Given this there will be many ways to analyze this data. It is our understanding that Dr. Liu and her team will also analyze and report on this symptom change data. We look forward to their analysis of this data.

As a part of this final report below we highlight our findings on 12-week changes for the major symptom categories.

- Pain and Movement Symptom Changes
  - There was a 57% reduction in overall pain, stiffness and mobility problems

- There was a 67% reduction in lower back pain in particular

- Menopause and Aging Related Symptoms
  - Frequent urge of voiding was reduced by -43%
  - Leak before reaching the toilet was reduced by -67%
  - Nighttime urination was reduced by -50-60%
  - Headache –72%
  - Insomnia –47%
  - Loss of Libido –41%
  - Difficulty in Intercourse –41%
  - Fatigue –36%
  - Vaginal Dryness –34%
  - Dry Skin/Wrinkles –35%
  - Mood Swings –33%

- Additional Benefits Reported
  - Finger and toe nail growth and strengthening, mentioned often.
  - Hair growth, mentioned occasionally.

Section # 3 Adverse Effects Section

A total of sixteen women participated in the symptom changes survey part of this twelve-week study. Fourteen women participated in the both the symptom changes and bone resorption segments of this study. All sixteen women took the same dose of Young Bones™, that is (2) 600 mg pills twice a day, for 12 weeks. All subjects used the Young Bones™ pills except Subject # 8 (Susan Brown) who is sensitive to the fillers and binders in the pill. She used the powder, one gram twice a day.

There were very few events reported which might in any way be considered as "adverse effects". One subject in the Later Menopause Group reported that she experienced a worsening of hot flashes while using Young Bones™. She also thought she developed headaches from the use of the product. Another woman in the Late Menopause Group reported a loose stool digestive problems, and she also reported she developed a sore developed under her nose while using Young Bones™.

Section # 4 Blood Chemistries to Date on Two Original Study Subjects To Have Measured, Bone Resorption, Bone Formation and BMD.

The last two subjects to enter the study (#8, SB and #14, DB) were subject to expanded testing. This testing included not only the serum NTX, but also testing of the markers of bone formation, osteocalcin and bone alkaline phosphatase, at several points

To date we have the data on the serum NTx, osteocalcin and bone alkaline phosphatase at baseline, 6 weeks and 12 weeks on these two subjects. Table #16 presents this data.

Table 16

Blood Chemistries on Last Two Study Subjects

Serum NTx				
	Baseline	6 weeks	12 weeks	6 months
Subject 14, Bixler	18.7	18.6	18.2	
Subject 8, Brown	12.7	12.9	9.5	

Osteocalcin				
	Baseline	6 weeks	12 weeks	6 months
Subject 14, Bixler	1.3	6.1	8.3	
Subject 8, Brown	4.6	4.1	4.8	

Bone Alk. Phos.				
	Baseline	6 weeks	12 weeks	6 months
Subject 14, Bixler	24.9	22.6	24.3	
Subject 8, Brown	8.6	8.4	10.1	

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While this data is incomplete, it is interesting in itself.

In subject # 14, Bixler, of the Early Menopause Group, bone resorption as measured by serum NTx was stable. Her bone formation, however, as measured by osteocalcin raised nearly 8 fold.

In subject # 8, Brown, of the Later Menopause Group, bone resorption as measured by serum NTx decreased significantly. Her bone formation, however, was near stable as measured by osteocalcin and rose only a little as measured by bone alkaline phosphatase.

Early in January 2004 we will have the final 6-month serum markers and the final 6-month BMD measurements on these two subjects.

Summary

As a whole the postmenopausal subjects using Young Bones™ experienced an increase in serum NTx from baseline to 6 weeks. From 6 to 12 weeks the group as a whole experience a trend toward decreasing NTx. Three of the fourteen subjects, however, displayed a significantly higher NTx at 12 weeks than at baseline.

We speculate that the rise in NTx from baseline to 6 weeks indicates the bone trophic effect of Young Bones™, causing both increase bone breakdown and increased bone formation. Given this, we would expect to see an increase in bone mineral density with Young Bones™ use.

As the previously given tables detail, the response to Young Bones™ varied to some degree among subjects. We suspect that Young Bones™ might act as an "adaptogen", bringing about the normalization of bone metabolism in accordance with the individual's biochemical needs. For example, when we looked at the bone formation markers along with the NTx bone resorption marker in two subjects interesting divergent patterns arose. In subject #14 the NTx was stable over 12 weeks, but bone formation as marked by Osteocalcin rise by nearly 8 fold. In subject # 8 bone formation was stable or rose just a bit as marked by bone alkaline phosphatase, but bone resorption declined significantly. Both biochemical patterns could be associated with an increase in bone mineral density. Early January 2004 we will have the six-month follow-up bone mineral density tests on these two women.

Finally, through this and other research projects we are beginning to think that the variability and insensitive of the Ostex NTx markers of bone resorption (serum and urine) are topics of concern in such small pilot studies. Given this new awareness, we now consider the bone mineral density test to be the most accurate and valuable measure of the effectiveness of any bone-building product. For details on this topic see Appendix #1.

Appendix # 1

While the serum NTx is supposed to be more precise and less variable than the urine NTx, still the coefficients of variation are still large. Given the day-to-day variation, the serum NTx requires at least a 14% change for "the least significant change". Even more we have discovered that the laboratory testing procedures themselves also allow for another large percentage (20%) variation within the testing procedures itself. Further there is also allowable variation in the mean absorbance value of the 0 standard and in calibration.
All this means that in small studies, very large changes must be seem to reach a level of true significance.

DETERMINING VALIDITY OF NTX TESTING

The following information on determining validity of NTx testing comes from the LabCorp Testing Guidelines Manual, 1998.

N-Telopeptide Serum Test

The following criteria must be met in order for the plate to be considered valid:

- The mean absorbance value of the 0 standard must be greater than or equal to 1.300.

- The span of the calibrator curve (absorbance difference between the 0 and 40 nM BCE calibrators) must be greater than or equal to 0.900.

- The % CV must be less than 20 to be considered as acceptable for anything pipetted in duplicate.