SJ BIOMED Inc.

Key Technology Highlights

Technology I: SJ-BRV Antiobesity Immunodrug

SJ-BRV is novel therapeutic and prophylactic immunodrug for the treatment and prevention of obesity by controlling lipid metabolism in a stage of storage. The key to the SJ-BRV vaccine is to trick the immune system into making antibodies against self antigens. SJ-BRV works by eliciting antibodies that block the binding of lipids in receptors in the adipose tissue thus preventing lipid storage in the adipose tissue.

- Working on process development on candidate protein SJ-BRV
- Formulation Study in preparation
- Preparing non-clinical toxicity study design and clinical design

Technology Overview

Technology I: SJ-BRV Antiobesity Immunodrug

SJ-BRV is novel therapeutic and prophylactic immunodrug in development for the treatment and prevention of obesity by controlling lipid metabolism in a stage of storage and clearance. SJ-BRV's pharmacological effects will be described under the clinical guidelines to treat overweight and obesity.

1. Efficacy of SJ-BRV

Body weight reduction in the range of 10% is associated with significant improvements in a wide range of comorbid conditions (type II diabetes and CVD). Thus vaccination of SJ-BRV on body weight increment was measured in 60% high fat induced obesity mice.

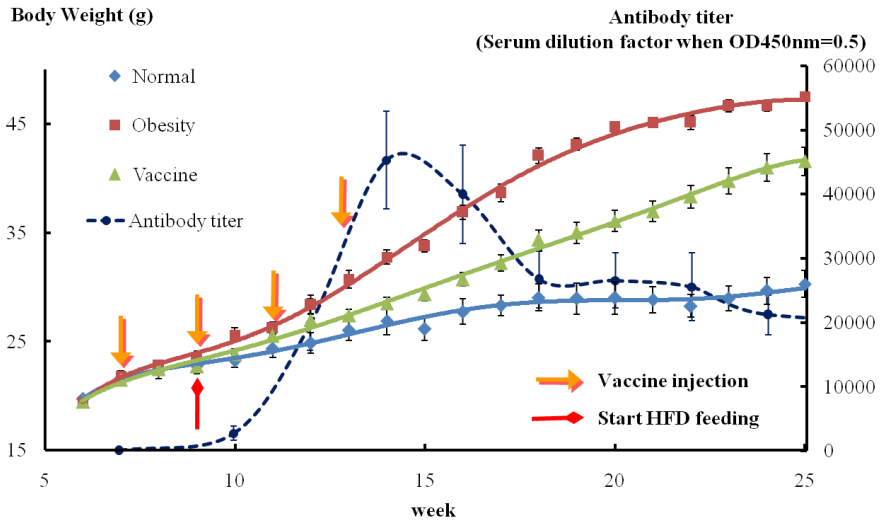

Fig. 1 Body weight change and Apo-B antibody titer after SJ-BRV vaccination

□ The vaccinated animals showed strongly suppressed body weight increments (up to 35%) compared with mock or control group animals as you see in a graph below.

□ Mice received vaccination didn't eat differently than the others suggesting that the vaccine slows the rate of weight gain while still allowing for normal eating habits.

Abdominal obesity, particularly visceral fat, is a better predictor of increased risk for cardiovascular disease and insulin resistance than overall body fat, thus effect of SJ-BRV vaccination on viceral adipose tissue was measured in C57BL/6J ApoE -/- mouse

□ Vaccination reduced viceral adipose tissue mass in C57BL/6J ApoE -/- mouse

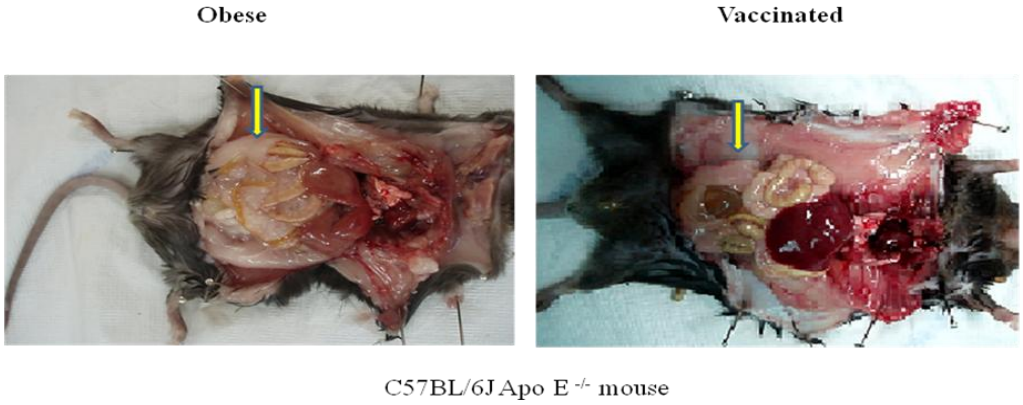

Fig 2. Abdominal fat mass in obese and SJ-BRV vaccinated

Obesity also contributes to the development of nonalcoholic fatty liver disease, nonalcoholic steatohepaitis, gallbladder disease, hypertension, cancer, and endocrine changes. These conditions are the result of downstream changes due to the increased metabolic activity of excess adipose tissue. The increased physical mass of adipose tissue in overweight or obese individuals causes a number of undesirable changes, including obstructive sleep apnea, altered pulmonary function, disease of the bones, joints, muscles, and connective tissue (eg, osteoarthritis), as well as skin laterations. Thus effects of SJ-BRV on fatty liver were investigated.

□ SJ-BRV vaccination reduced fat accumulation in the liver

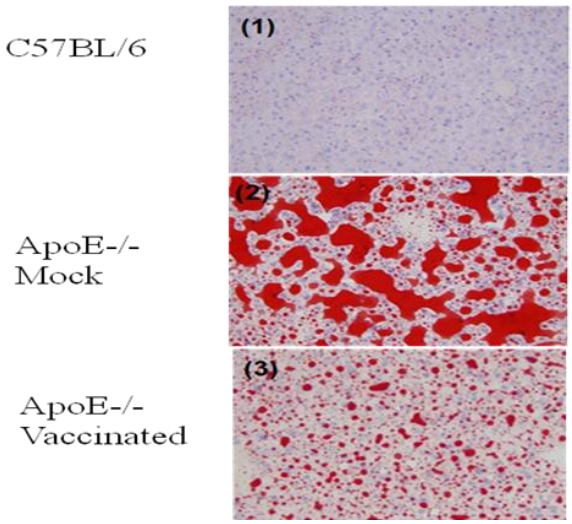

Figure 3. Oil Red O staining in Liver in C57BL/6J ApoE -/-

In addition to those parameters, other signs and symptoms of obesity include insulin resistance, increased glucose levels, increased blood pressure, elevated cholesterol and

triglyceride levels, decreased levels of high density lipoprotin cholesterol (HDL-C), shortness of breath, and back pain. Some of those parameters were measured but needs to be repeated on a efficacy maximization process and some of those parameters are not examined yet but under the study. Parameters available will be summarized detail later.

Considering body weight reduction in the range of 10%, abdominal adiposity reduction and/or fatty oil are associated with significant improvements in a wide range of comorbid conditions (type II diabetes and CVD), vaccination of SJ-BRV has potential to be developed as a good anti-obesity vaccine candidate.

2. Mechanism of Action (Novel mechanism of action)

SJ-BRV is novel therapeutic and prophylactic immunodrug for the treatment and prevention of obesity by controlling lipid metabolism in a stage of storage. Apolipoprotein B-100 is a crucial molecule at the transport, receptor-mediated storage, lipase activity, for the metabolism of triacylglyceride and cholesterol. For the lipid metabolism, absorption, transport, and storage of lipids from intestinal contents take place in a series of interrelated steps including emulsification, hydrolysis by specific esterases, lipases, micelle transport, mucosal absorption, re-synthesis of parental molecules in enterocytes, and assembly with apolipoproteins. Also at the peripheral uptake and storage of lipids by specific receptors and all of these steps can be potential therapeutic targets in the treatment of obesity. ApoB as a lipoprotein portion of LDLs, it has an important role in the uptake of lipids in LDL receptors at the peripheral adipose tissues.
Vaccination of SJ-BRV induced high levels of apolipoprotin B-specific antibodies. ApoB antibodies bind to apoB in the circulating fats and thus inhibit or reduce uptake of lipids by blocking (V)LDL receptors at peripheral adipose tissues.
In addition it stimulates the macrophage mediated clearance of lipids from peripheral circulation. Impede the access of plasma lipoprotein lipases to VLDL and LDL thus, sterically inhibits the lipoprotein lipase activity.
The key to the SJ-BRV vaccine is to trick the immune system into making antibodies against self antigens. SJ-BRV works by eliciting antibodies that block the binding of lipids in receptors in the adipose tissue thus preventing lipid storage in the adipose tissue.

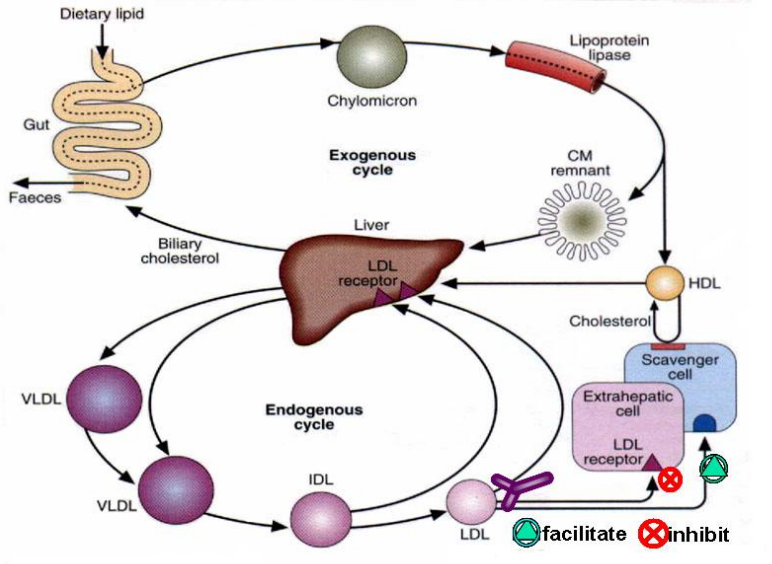

Fig 3. SJ-BRV's mechanism of action

3. Key advantage of our technology

(1) Novelty and rationale for mechanism of action
(2) Competition within the marketplace
Most drugs developed and currently developing are seeking to modulate obesity-driven receptors via agonist or antagonist which have been remarkably unsuccessful. They are effective only while treatment is maintained and when treatment stops, weight returns..
When you diet, the body responds as if it was starving and set the body homeostasis to slow down fat metabolism and stimulate eating by compensation mechanism to save life. Those change help body to retain and regain fat. As a result, many people end up regaining the weight they lost and more once they go off their diets. Vaccination of SJ-BRV may have the advantage to prevent or seriously reduce yo-yo dieting since it does not affect appetite and create starvation condition in a body but prevent accumulation of fat and increase clearance of fat in a last stage of metabolic pathway. The use of SJ-BRV vaccines to induce autoantibodies that neutralize disease-related proteins offers a means to effectively and affordably treat obesity.
(3) Research approach to achieve best clinical results and to meet the commercialization criteria. More pharmacological and toxicology data associated with risks and benefits will be made based on research approach likely to achieve best clinical and commercial results.

Table 1. Strength and weakness for current therapy

Strength	- 4 times every 2 weeks and then every 6 month - Good efficacy is expected based on the efficacy in DIO (HFD 60%) - Patent expiry will be later than 2032 - Highly safe and effective - User friendly treatment - Eat as you want!
Weakness	-Not found
Opportunities	- Novel mechanism - European charter on counteracting obesity - Enjoy over 20 years of global patency
Threats	- Qß-GIP (cytos) - OTC chemicals

- Xenical (lipase inhibitor and blocks the absorption of dietary fat in the intestines): unpleasant gastric side effects, oily stools and urgency
- Sibutramine (5-HT reuptake inhibitor) : dry mouth, headache, insomnia,, constipation and increased blood pressure, In USA, 49 cardiovascular death
- Rimonabant (cannabonoid receptor 1 antagonist -inhibits brain receptors involved in eating) :drug also inhibits other areas of the brain and other organs, raising serious concerns about the drug's toxicity

Although there are other drugs under development with known targets such as lipase inhibitors (Cetillistat by Alizyme/Takeda, lorcaserin (APD-365 by Peptiimmune /Genzyme), we think that our competitor is Cytos's Qβ-GIP

4. Competitor to SJ-BRV : Cytos's Qβ-GIP vaccine

Drug candidate's evidence for the treatment of overweight and obesity can be assessed for the following five criteria; weight, abdominal fat, glucose intolerance, dyslipidemia and high blood pressure. Effects of drug candidate in those parameters are very important to assess its

proof of concept in clinical trials. SJ-BRV's competitiveness to cytos's Qβ-GIP will be compared under those parameters.
Qβ-GIP obesity vaccine is targeting peptide hormones named insulinotropic polypeptide (GIP). Although Qβ-GIP is anti-obesity vaccine targeting protein involved in the disposal of both glucose and fat, it is gut hormones aiding fat deposition and triglyceride accumulation in adipose tissue. As explained above, hormone is involved in the body homeostasis so when it's function is modulated, compensation mechanism occur in the body leading yo-yo phenomenon when treatment is stop. In that sense hormone is not a good target for the long term obesity treatment.

Cytos's anti Qβ-GIP	Comparison	SJ Biomed' SJ-BRV
GIP vaccine		SJ-BRV vaccine
100ug 2-weeks interval 4 times injection SC	Dose Injection interval Injection times Route	50ug 2-weeks interval 4 times injection IP
35% 22-26% reduction No difference No difference ND	Body weight Abdominal Fat Glucose intolerance Dyslipidemia High blood pressure	Decrease Decrease ND No difference ND

• Glucose parameters: glucose intolerance, HbA1c, fructosamine, glucose levels
• Lipid parameters: total cholesterol, low density lipoprotein (LDL), high density lipoproteins (HDL), free fatty acid (FFA), triglyceride (TGs)
• ND not determined yet

SJ-BRV's route optimization and efficacy maximization is currently undergoing. More results will be available soon.

5. Developmental Status

Currently we are working on process development for large scale up manufacturing to provide non-clinical toxicity and formulation study materials.
For detailed developmental plan, please see the table below.

Table 2. SJ-BRV developmental time line and ball part cost estimate

	2011				**2012**				**2013**			
	Q				**Q**				**Quarter**			
	1	2	3	4	1	2	3	4	1	2	3	4
Manufacturing												
Large scale up process development and analytical method development												
Preformulation study												
Non-clinical tox material production												
Non-clinical tox study												
Pre-Pre IND meeting with FDA CBER												
Formulation study												
Clinical batch DS production												

Clinical batch DP production												
Pre IND and IND												
Clinical Trial Either safety, tolerability and dose finding (Phase I, IIa)												

Clinical testing plans, time table and cost estimates

Since we are working on large scale manufacturing and haven't even finished non-clinical toxicity study yet, we don't have exact clinical design yet thus no cost estimates yet. However we know what to get and where to go as described above. Guideline suggest to examine the scientific evidence of candidate to overweight and obesity, it should be related to 1. other heart disease risk factors, such as hypertension, blood lipid levels, and diabetes; 2. the distribution and amount of body fat as it influences risk; 3. the independent relationship of obesity to coronary heart disease (CHD); and, 4. the relationship of obesity to sleep apnea. We will accumulate those data until we enter clinical trial to better design to get proof of concept with less risk of side effects in human.

6. Cost Estimate

Year 2011 : Total 2 million$
Process development,
Non clinical toxicity study material production,
Formulation
Efficacy Optimization

Year 2012 : Total 2.1 million$
Non-clinical toxicity study in animal
Clinical material production (DS & DP)
Clinical trial protocol
Pre-IND and approval

Patent Information

Title	Status	Country	ID No	Date
Mimetic Peptides for epitope of apolipoprotein B-100, concatemer and modified peptides thereof, and the vaccine composition comprising the same.*	Registered	U.S.A.	6,825,318 B2	2004.11.30.
		Korea	0472841	2005.02.14.
		China	CN1231262C	2005.12.14.
		Russia	2313536	2007.12.27
		Europe	1315517	2010.10.20
		Australia	2007200834	2009.09.29
	Pending	Japan	2002-524523	2002.05.01
Anti-obese	Registered	Korea	10-0639397	2006.10.20

immunogenic hybrid polypeptides and anti-obese vaccine composition comprising the same		Australia	2005222019	2008.05.15
		Russia	2341534	2008.12.20
		India	226614	2008.12.22
		Japan	4554672	2010.07.23
		U.S.A.	7,829,667 B2	2010.11.09
		Mexico	PA/A/2006/010635	2010.10.06
		China	200580008711.2	2010.12.02
		Canada	2,560,539	2011.01.11
	Pending	PCT	KR2007/004692	2007.09.21
		Europe Brazil	05 721 957.8 PI0508916-6	2006.10.17 2006. 09.18
Anti-obese immunogenic hybrid polypeptides and anti-obese vaccine composition comprising the same**(II)**	Registered	Korea	10-0956893	2010.04.30
			19-0970178	2010.07.07
		Russia	2009115688	2010.11.12
		Europe	07808454.8	2009.04.27
		Australia	2007300842	2011.01.27
	Pending	Brazil	0717223-0	2009.03.24
		Canada	2,664,529	2009.03.25
		China	200780035653.1	2009.03.25
		India	2104/CHENP/2009	2009.04.17
		Japan	2009-5291322	2009.03.24
		Mexico	MX/a/2009/003188	2009.03.24
		U.S.A	12/442,760	2009.03.25
		PCT	WO2008/038990	2008.04.03