Therapeutic drug for Alzheimer's disease targeted beta-amyloid aggregation/ toxicity blocker

Medifron_DBT

Contact Information

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Industry Sector	Drug discovery, Pharmaceutical
Therapeutic Area	Central Nervous System
Stage of Development	Phase I

1. Summary

- Alzheimer's disease (AD) is worldwide 4th causing death
- Number of AD patient increase rapidly coming after elderly society
- Most of dementia is AD (over 60%)
- The causing agent for AD is believed beta-amyloid peptide
- In the brain, beta-amyloid over produced and make plaque outside neuron
- Beta-amyloid in plaque is very resistance to protease attack
- Solubilized beta-amyloid can be transfer to BBB through LRP receptor and eventually degraded
- DWP09031 showed aggregation inhibitor as well as toxicity blocking activity
- Proof of concept done by transgenic animal model

2. Applications

- Neurodegenerative disease caused by protein aggregation
- Alzheimer's disease

3. Market Feasibility

- Global AD market reach to 10B US$
- In US, every year over 100B US$ spend AD care cost
- Disease modification drug can be developed and it will expend market size

4. Type of Business Relationship Sought (include licensing availability)

- We are actively seeking partner for global clinical trials.
- Out licensing deals for world exclusive sales right except Korea

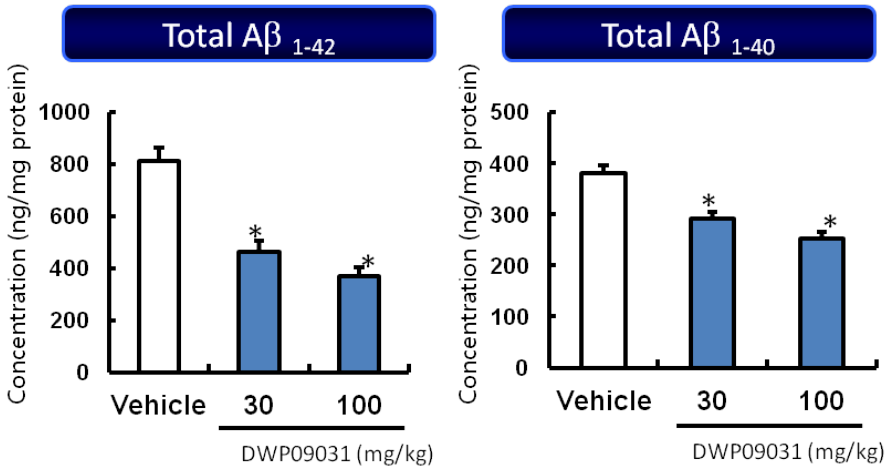
5. Technical Advantages

- Drug candidate for aggregation/toxicity blocker
- DWP09031 is to bind beta-amyloid peptide and block aggregation of beta-amyloid, therefore toxic form of oligomers of beta-amyloid could not be formed and soluble beta-amyloid might be transported outside the brain via LRP, scavenger receptor of brain.
- Using hippocampus, DWP09031 can be restore LTP(long term potentiation) after beta-amyloid challenge

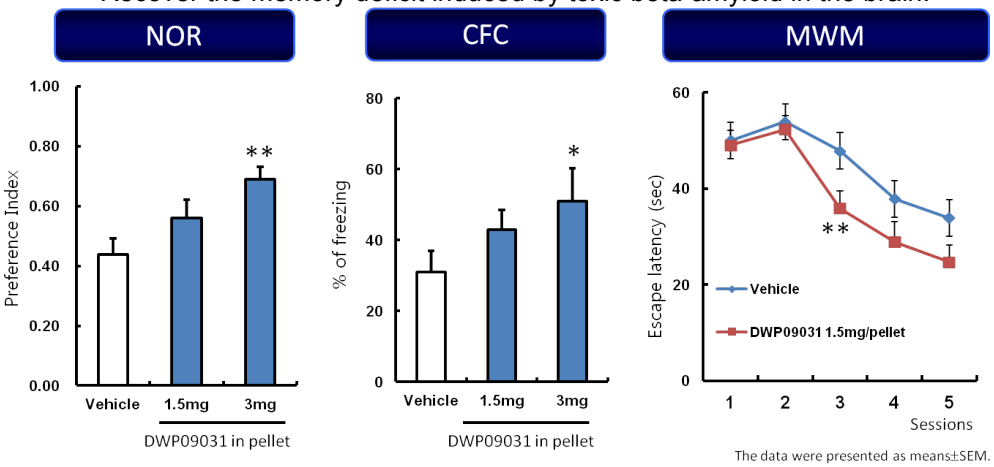
- In animal model, the concentrations of beta-amyloid are lowered by 50% in the brain and recover the memory deficit induced by toxic beta-amyloid in the brain.
- Human clinical trial study results showed that maximum dose (single dose 2,000mg) did not showed any sign of toxicity.

6. Technical Highlighted Summary

- The concentration of beta-amyloid is lowered by 50% in the brain after treatment of DWP09031



- Recover the memory deficit induced by toxic beta-amyloid in the brain.



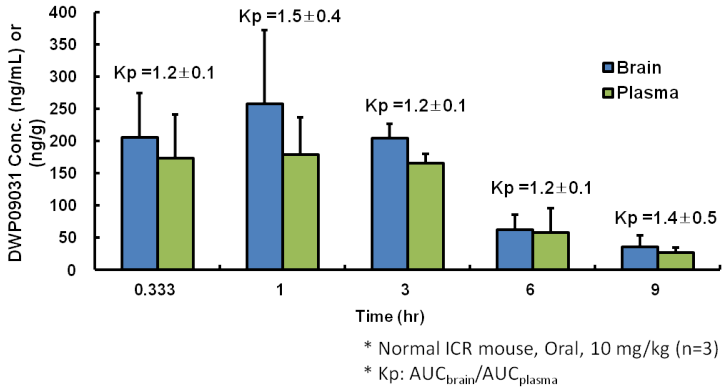
*Novel objective recognition (NOR), Contextual fear conditioning (CFC), Morris water maze (MWM)

The data were presented as means±SEM.
n=8 / group, One way ANOVA followed by LSD t-test
[* p<0.05, ** p<0.01: compound vs. vehicle]

- Relatively high bio-availability in rodent and non rodent species

Systemic PK	Mouse (10mg/kg)	Dog (10mg/kg)
F %	52	65

- Good BBB penetration profile of DWP09031. Over 20% more compound detected in brain than plasma



- Less drug drug interaction prediction. Seven isoforms of CYP enzyme cannot inhibited by DWP09031

Human CYPs	IC_{50} (uM)
1A2, 2A6, 2C8, 2C9, 2C19, 2D6, 3A4	over 30

- GLP-compliant safety studies on rodent and non rodent including 4 weeks repeated dose toxicity, genotoxicity and safety pharmacology were done.
- More importantly, in vitro hERG channel study showed low binding potential.
- No moderate and significant safety issues occurred during safety and toxicity studies.

7. Mechanism (MOA)

- Small molecule direct bind to beta-amyloid
- Small molecule inhibit aggregation of beta-amyloid and block toxic effect of beta-amyloid
- Protect brain damage caused by beta-amyloid challenging

8. Patent Information and Status

- Medifron_DBT filed patent
- Medifron_DBT has all commercial right for DWP09031
- Process development patent also filed

9. Patent Number(s)

Title	Country	Patent Application No.	Original Assignee	Filing Date	Inventors

Composition comprising benzofuran type derivative for treating and preventing cognitive dysfunction	**KR** **JP** **CN** **US** **EP**	10-0858357 (registered) 5392776 (registered) ZL200780036324.9 (registered) 8,263,649 (registered) 07833146.9 (filed)	Medifron_DBT	2006.10.02 2009.03.11 2009.03.30 2009.04.01 2009.03.16	J Lee, DW Kang, YH Kim, H Kim, HJ Ha, EJ Nam, CM Chung
Process for the preparation of benzofuran derivatives	**KR** **ID** **CN**	10-2013-0078550 (filed) [priority10-2012-0073551/2012.07.05]	Medifron_DBT	2013.07.04	SJ Choi, BG Lee, HK Yoon, YM Lim, JH Lee, SW Park

10. Key Words

- **Beta-amyloid, aggregation inhibitor, toxicity blocker, Alzheimer's disease, recover brain function, clinical trial**

11. Company Description

- In 1999, the company spun off from Seoul National University, School of Medicine and School of Pharmacy in order to commercialize intellectual property and asset of academia for Alzheimer's disease and neuropathic pain.
- In 2002, Korean Government nominated the company as NATIONAL CENTER for Alzheimer's Disease DRUG DEVELOPMENT
- Medifron_DBT and Grunenthal GmbH, Germany based pharmaceutical company made a license and research collaboration agreement on TRPV1 antagonists, so called target based license in year 2005 and 2007 additional licensing deal made
- In 2008, Medifron_DBT and Daewoong pharmaceutical company made an agreement for Alzheimer drug co-development
- In 2010, Swiss based pharmaceutical company Roche and Medifron_DBT, Inc. have entered into an agreement of Research Collaboration and License on RAGE antagonists for Alzheimer's disease treatment.