# Novel SN-38 Derivatives

~ A Nano Carrier-free Prodrug for High Anti-Tumor Activity and Safety ~

### **KEY INVENTION**

- A prodrug utilizing SS bond reduction by glutathione (GSH) localized in tumors
- A nano carrier-free DDS designed by making the drug itself into nanoparticles
- For development of a novel drug showing a high anti-tumor activity and safety!

(A medical doctor-led clinical trial is expected to be carried out.)

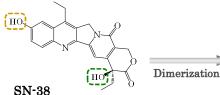
[Disadvantage of Current Nano Carriers and Prodrugs] [Advantage of SN-38 Derivatives]

- Nano Carriers (LNP, etc.)
  - High Liver Accumulation (>90%)
  - Low API Loading (<10%)</li>
  - Side Effects by Carriers (other than API)
- - · Low efficacy and side effect by metabolism before delivery to the target cells



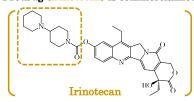
- **High Target Cell Accumulation**
- **High API Loading**
- Nanoparticles by Drug Itself (No Carrier)
  - Poorly metabolized before delivery to the target cell (metabolized by GSH)

### SUMMARY of INVENTION



#### SN-38

- · Topoisomerase Inhibitor
- · Low Water Solubility (<5 ppm)
- · Prodrug (Irinotecan) is commercialized.





#### SN-38 Derivatives (SN-38 SS Linker Dimers)

- · SN-38 Dimers through SS Linker including an SS Bond
- · Prodrug utilizing SS Bond Cleavage (Reduction) by GSH
- · Less impact on normal cells due to less GSH in the cells

**High Dispersion Stability** 

## COMPARISON with and ADVANTAGE over CURRENT TECHNOLOGY

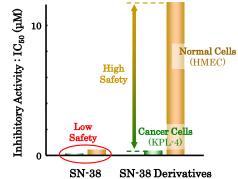
[Efficacy and Safety Comparisons of this Technology with Current Technology]

a. in vivo Trial (Mice 1), i.v.)

1) HCT116 (from Human Colon Cancer) Tumor Cell-bearing Mice 2) Dose: 10 mg/kg/day Relative Tumor Volume 30 Control 20 10 J SN-38 Derivatives 30 Days after Administration (day)

The anti-tumor activity of SN-38 derivatives is higher than that of Irinotecan.

b. Safety (SN-38 vs. SN-38 Derivatives)



The safety of SN-38 derivatives is higher than that of SN-38.

# APPLICATION expected

Development of Novel Anti-Cancer Drugs such as for Lung, Breast, Colorectal, Cervical or Stomach Cancers

Representative Inventor:

Title of Invention:

Co-Inventor: Licensable Patent

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SN-38 Derivatives, Nanoparticles including the Derivatives, Medicines and Production Methods of the Nanoparticles

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