

## IIIM-284N

[IIIM(N)-284/14 (Target: Tubulin polymerization)]

It is a semi-synthetic derivative of a natural product colchicine. It possess better therapeutic window than a parent natural product colchicines. It has reduced P-gp induction liability than colchicine (Pgp induction  $EC_{50}$  of IIIM-284 and colchicine is 69 and 14.4 nM, respectively). It possess excellent oral bioavailability (64% F) in BALB/c mice (10 mg/kg p.o.:  $t_{1/2,\beta}$  = 5.43 h;  $AUC_{0-t}$  = 16899 ng•h/mL;  $AUC_{0-\infty}$  = 17334 ng•h/mL;  $C_{max}$  = 3031 ng/mL;  $t_{max}$  = 2 h). It showed promising in-vivo efficacy in murine models: Ehrlich solid tumors (%TGI): 2.0 mpk P.O. = 38 (mortality = 0/7); P388 lymphocytic leukemia (%T/C): 1 mpk i.p. = 174.3(significant activity); L1210 lymphoid leukemia (%T/C): 1 mpk i.p. = 231.7 (significant activity). This lead is presently under in-vivo validation in human xenograft models.