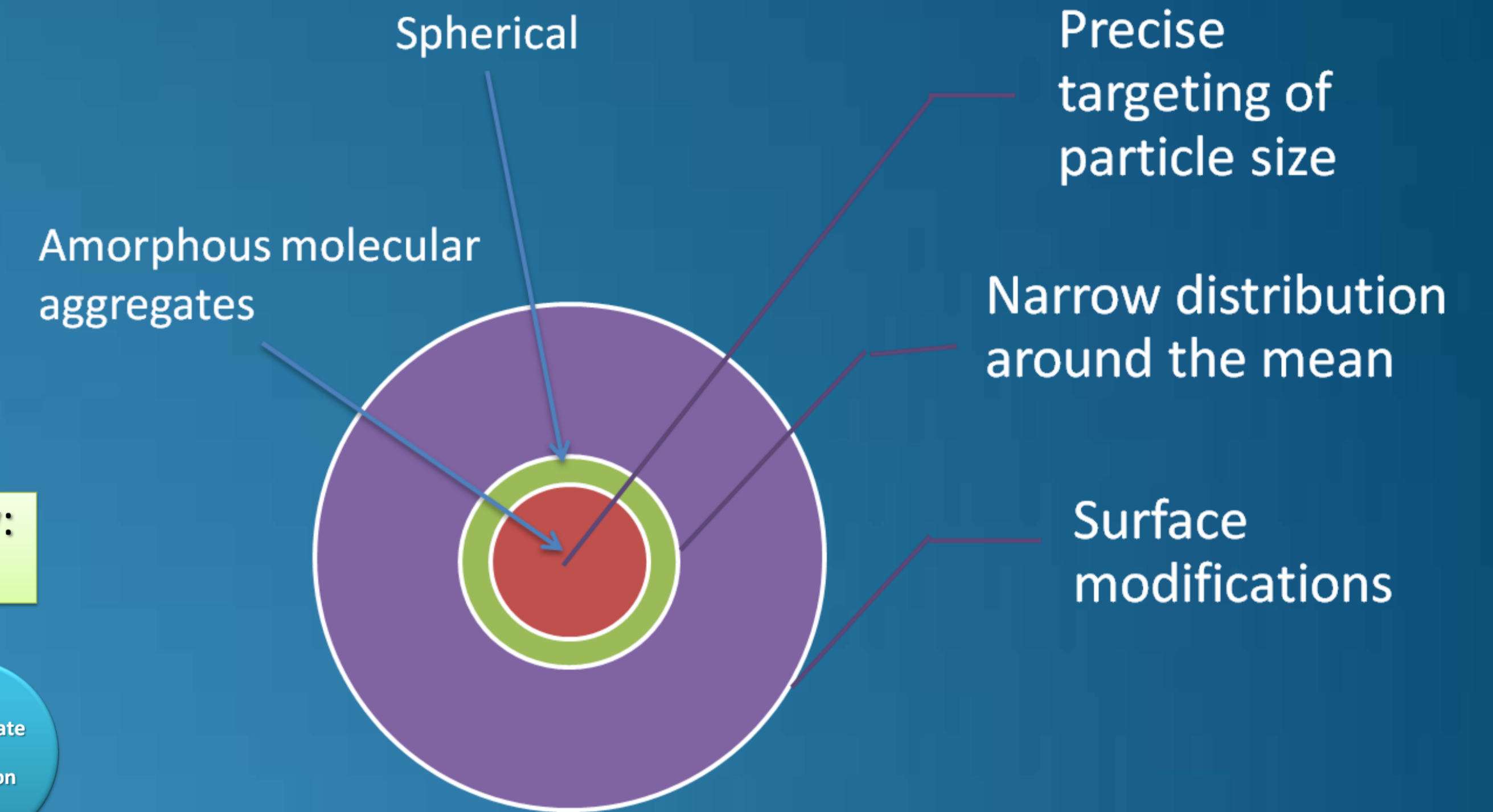


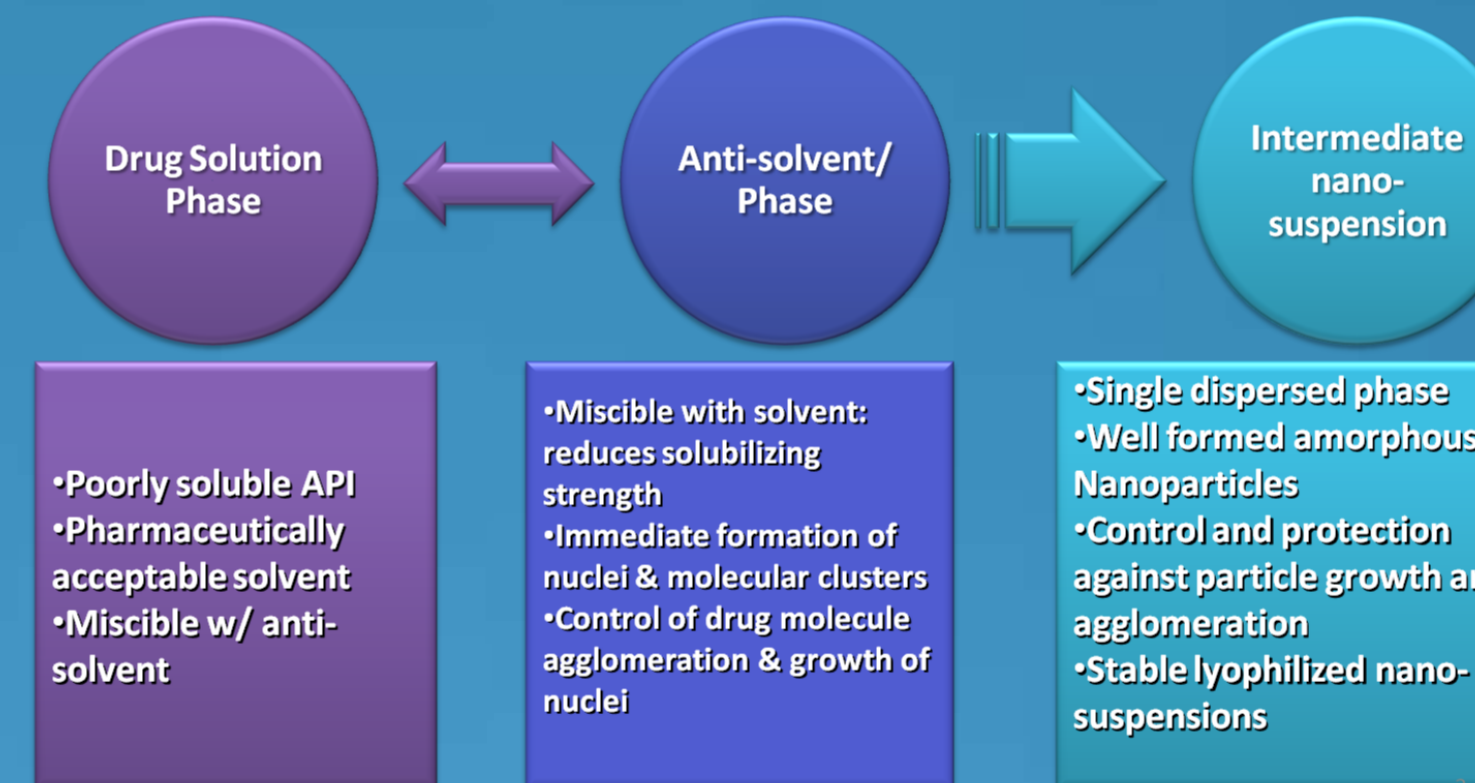
## NovaSpense<sup>SM</sup> Technology

### ABSTRACT SUMMARY

Poorly water soluble compounds are difficult to develop as drug products using conventional formulation techniques and are frequently abandoned early in discovery. NovaSpense<sup>SM</sup> is a bottom-up proprietary process which develops surface-modified, targeted nanoparticles of poorly soluble compounds. Using the process, a nanoparticulate suspension of an estradiol analog was developed. Pharmacokinetic studies of the nano-suspension with surface modified nanoparticles indicate a twenty fold increases in the circulatory half-life against that of a drug solution.



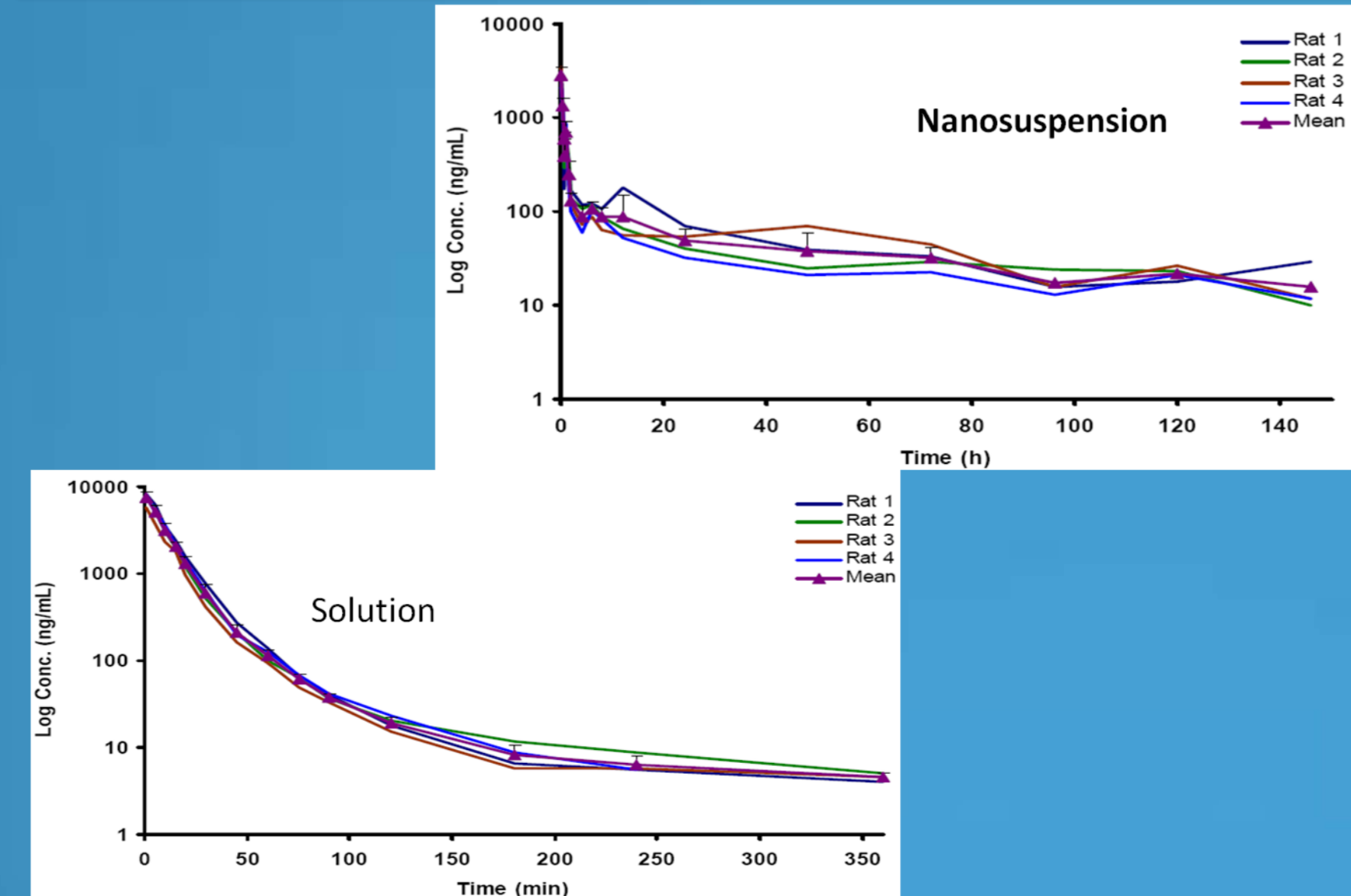
### NovaSpense Nanoparticle Technology: Process Principle



### Smart Nanoparticles of Estradiol Analog : Pharmacokinetics

Parameter	Solution	Nanosuspension
T <sub>1/2</sub> (hr)	2.5	54
C <sub>max</sub> (mg/L)	7.6	2.8
AUC <sub>(3 half-lives)</sub> (mg*hr/L)	1.6	6.7
AUC <sub>(infinity)</sub> (mg*hr/L)	1.6	7.8

### Smart Nanoparticles of Estradiol Analog : Pharmacokinetics



### RESULTS AND DISCUSSION

Product potency was assayed on reconstituted samples by HPLC. Lack of crystallinity was initially assessed by the absence of birefringence to polarized light microscopy and was confirmed by x-ray diffraction. Nanoparticles sphericity was confirmed by transmission electron microscopy. Stability of the lyophilized product to particle size growth has been confirmed for 15 months at room temperature storage.

Average particle size of the nano-suspension was 105nm at the time of manufacture and 87nm when reconstituted from the lyophilized product to 3mg/ml with room temperature water. The reconstituted nano-suspension remained viable for at least 12 hours when stored at 5°C.

Pharmacokinetic evaluation of the formulation in cannulated rats versus a solution of the same active showed a half-life of 54 hours versus 2.5 hours. The data was normalized to the same dose administration.

### CONCLUSION

The NovaSpense<sup>SM</sup> process develops and precisely controls the formation of amorphous, spherical surface modified nanoparticles. The proprietary process has been used to develop surface modified nanoparticles of poorly soluble drugs for several routes of administration which are undergoing *in vitro/in vivo* trials to establish their efficacy.

