PARTICLE SCIENCES

DRUG DEVELOPMENT SERVICES

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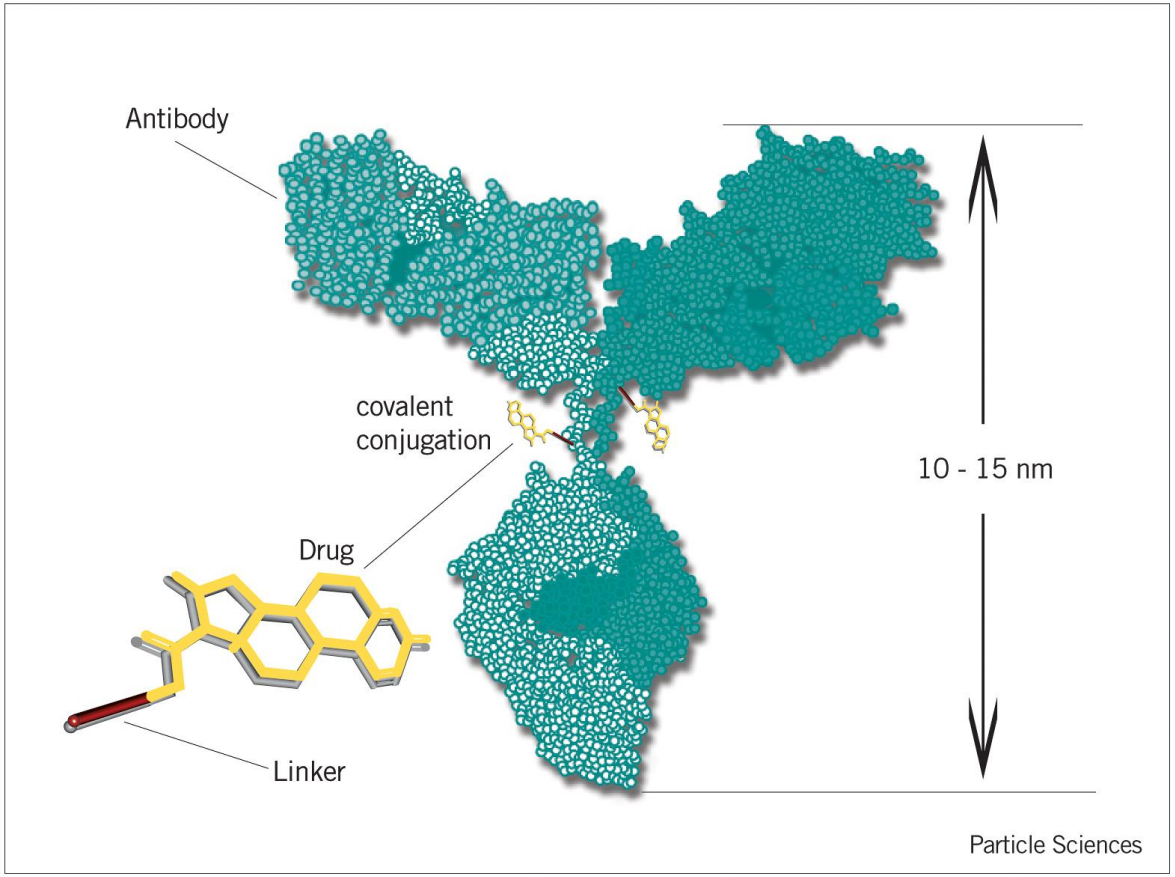
Drug Delivery Technologies

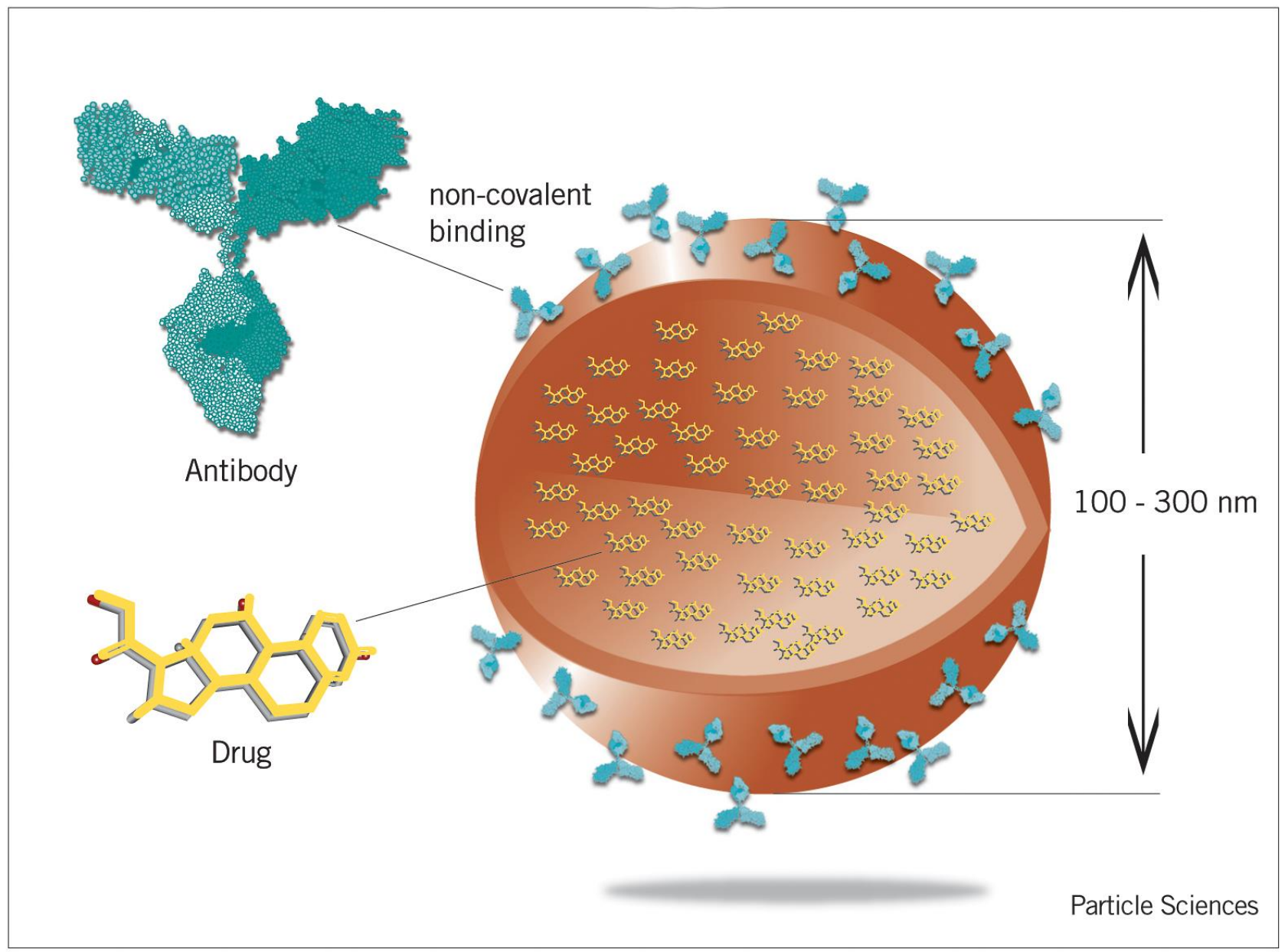
- Antibody-Drug Conjugates (ADC)
  - Providing antibody (Ab) specificity to drugs
    - Relies upon proprietary covalent linkers
- Nanoparticles +/- PEGylation
  - Highly versatile
  - Affects both biodistribution by enhanced permeability and retention (EPR) effect, and bioavailability
  - Can provide sustained drug release
- Surface Arrayed Therapeutics™ (SATx™)
  - Combines Ab specificity and nanoparticle versatility
  - Nanoparticles composed of solid-lipids with modified surfaces
    - Readily incorporates hydrophobic drugs
  - Particles' surfaces customized for non-covalent binding of targeting molecules and biopharmaceuticals
    - Including human monoclonal Ab

Typical ADC Products

- Dependent on covalent linkers
  - Must cleave linker to release drug in the cells
  - Complicated regulatory path
- Limited array of suitable drugs
  - Amendable to protein conjugation
- Low drug loading on Ab
  - Requires high potency drug
    - Picomolar activity
  - Applicable only to disease targets with high copy number antigens (Ag)
  - Needs to be internalized by target cells to liberate drug
  - Probably not amendable to extracellular delivery



The SATx™ Platform



SATx™ Attributes

- Drug Loading - Payload
  - Solid-lipid particles suitable for broad portfolio of drugs
    - Publications demonstrate applicability for over 500 drugs
    - Composed of common, safe components
    - Potential high drug loading and delivery
      - Tunable within particles and not limited by drug to Ab ratio
- Targeting
  - Surface of SATx™ can be customized to bind drugs, biological ligands and biopharmaceuticals, including antigen specific antibodies.
    - Particles' surfaces modified with safe and standard cationic, anionic and neutral modifiers
  - Further enhanced by well known EPR effect

SATx™ Examples

- Use surface modifiers that mediate non-covalent binding to proteins
- Charged and neutral modifiers can be mixed to optimize SATx™ particles for specific applications
- Mean particle sizes are typically between 100 – 300 nm in diameter

Formulation	Zeta Potential	Mean Particle Size
A	-12.8 mV	298 nm
B	+78.1 mV	248 nm
C	+78.0 mV	178 nm

Example: Human IgG1

Predominant Class for Human Monoclonal Antibodies

- Heavy Chain Type
  - γ1
- Molecular Weight
  - 146,000
- Hinge Region Amino Acid Number
  - 15 amino acids
- Charge
  - Isoeletric point of pH 8.6 ± 0.4
  - Has a net cationic charge at physiological pH

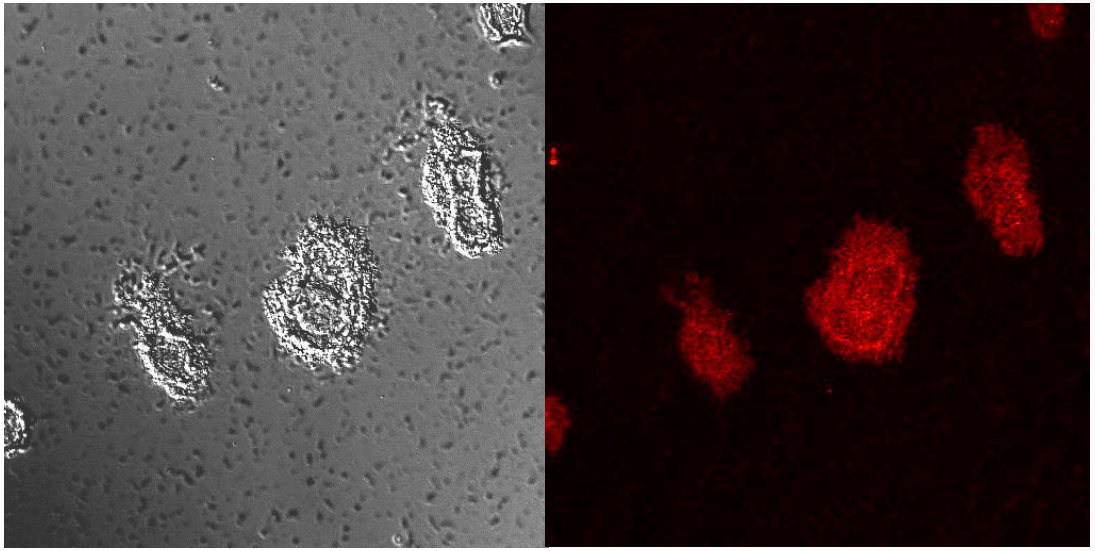
Human IgG1 Binding to SATx™

Formulation	Bulk Molar Ratio of Surfactant/Ab for 100% binding	Impact of Strong Ionic Solutions
A	35.2 – 3.5	+
B	6,300	++
C	< 63	None

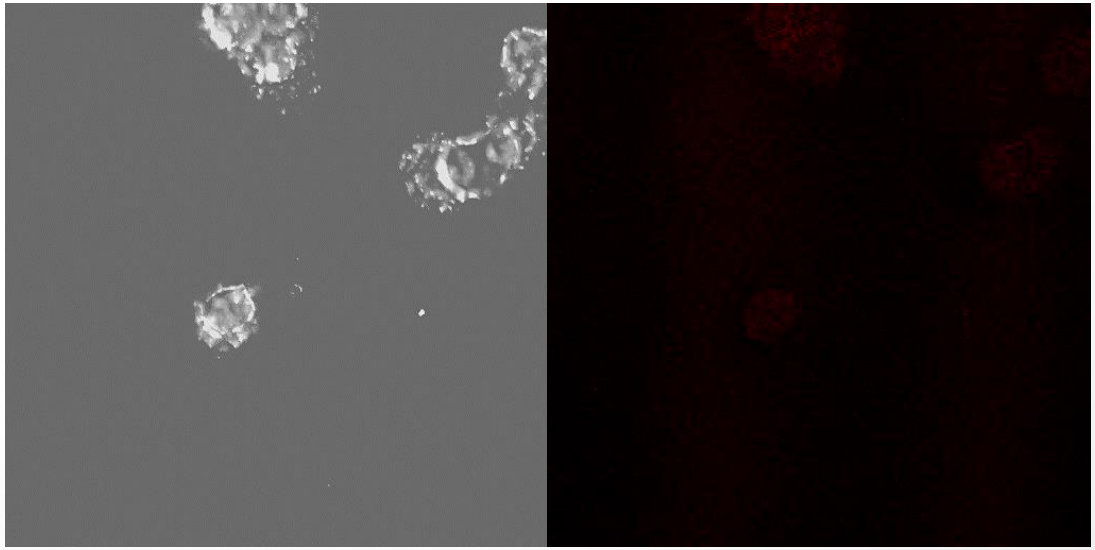
Targeted SATx™ – Cell Binding

- Fluorochrome loaded SATx™ particles arrayed with humanized anti-tumor Ag monoclonal IgG1 antibody or non-specific human IgG1
- Incubated with tumor cell lines and evaluated by fluorescence microscopy
- Antigen specific SATx™ particle binding
- IgG1 control SATx™ particles did not bind to tumor cells

Tumor Cell Line – SATx™ Coated with Specific IgG1



Tumor Cell Line – SATx™ Coated with Control IgG1



SATx™ is a Flexible Platform

- Accommodates a broad array of drugs and biopharmaceuticals individually and in combinations
- Completely tunable ratio of combined components
- Non-covalent linking biological ligands with other drugs
  - Minimizes regulatory burden
- Extracellular and intracellular delivery
- Sustained release of drugs and biopharmaceuticals
- Multi-functional formulations
  - Including multiple Ab specificities for cross-linking target Ags
- Vaccine formulations – essentially creating synthetic VLP
  - Links vaccine antigens to immunomodulators, like TLR agonists

Concept to Clinic.

We Deliver®