PSVue®, reagents are a family of fluorescent probes containing a bis(zinc²⁺-dipicolylamine) group (Zn-DPA), a motif that has been found to bind with high selectivity to surfaces enriched with anionic phospholipids, especially phosphatidylserine (PS) exposed on cell membranes. The fluorescent part of the probe is a reporter element that provides a means of detecting the probe once it is bound to the membrane of interest.

Key Features of PSVue® Probes:
- Bind to a variety of cell types which have negatively charged phospholipids exposed on their membranes including apoptotic Cells, necrotic cells, Gram+ and Gram- bacteria activated cells, tumor vascular endothelial cells, viruses, etc.
- Available in a range of detection wavelengths from long-UV to near infrared.
- Suitable for in vitro and in vivo use.
- Suitable for high-throughput screening assays.
- Bind to the same PS site as annexin-V.

Advantages of PSVue® over Fluorescent Annexin-V:
- Binding kinetics are fast; annexin-V binding is slow
- Binding is Ca²⁺ independent; means no artifacts due to activation of nonspecific membrane scramblases by Ca²⁺
- Cheap compared to most annexin-V fluorescent analogs
- Apoptosis can be detected under a wide variety of conditions (e.g. in presence of 10% serum, temps from 4 to 37°C)
- Can provide more intense labeling due to their much smaller size (i.e. >10 PSVue® molecules can bind to the same area as 1 annexin V molecule)

General Structure of PSVue® Probes (Figure 1)

In Vitro Studies:
Several in vitro studies have shown that PSVue® compounds stain the same apoptotic cells as fluorescently labeled annexin-V indicating that they are excellent small molecule mimics of annexin-V. An example using PSVue® 794 is shown in Figure 2.

Figure 1. Proposed Model of Membrane Binding:
Figure 3 illustrates the 3 component assembly process that results in high affinity association of PSVue® with PS-rich membranes. Under physiologic concentrations of Zn²⁺ the predominant coordination complex is the mono-zinc species (species A). The binding of species A to the anionic PS exposed membrane (species B) would promote the binding of the second Zn²⁺ with subsequent binding to the membrane forming a bivalently bound species C. PSVue® reagents are selective for membrane phosphates and do not stain the cytosol.

Selected In Vivo Studies:
The in vivo images below show that in animal models of prostate cancer (Figure 4) mammary cancer, (Figure 5) bacterial infections and (S. aureus) (Figure 6), PSVue® targeted to the disease site.

Figure 2. Micrographs (60X magnification) of Jurkat cells, treated with cytotoxic camptothecin (10 μM) for 3.5 h and stained simultaneously with Annexin V-Alexa Fluor 488, and PSVue® 794 (10 μM), Brightfield image of the entire field of cells (A); cells stained with Annexin V-Alexa Fluor 488 (B); cells stained with PSVue® 794 (C); overlay of images A, B, and C (D). No staining of healthy cells was observed in the absence of camptothecin. (Images courtesy of Dr. Bradley Smith of University of Notre Dame)

Figure 4. X-ray and fluorescence overlay image of a rat prostate tumor model at 24 h postinjection of PSVue® 794 (4.0 mg/kg) shows clear evidence of selective accumulation in the tumor. The image was acquired at a 190 mm field of view. (Image courtesy of Dr. Bradley Smith of University of Notre Dame)

Figure 5. Representative overlay image of a nude mouse with an EMT-6 mammary tumor. Brightfield and fluorescence intensity images were acquired 24h following injection of PSVue® 794 and show clear evidence of selective accumulation in the tumor. The image was taken at a 80 mm field of view. (Image courtesy of Dr. Bradley Smith of University of Notre Dame)

Figure 6. Optical image of a mouse with a S. aureus infection in the left rear thigh muscle. Images were acquired before (A), and immediately following (B), iv injection of PSVue® 794 and at 6h (C), 12h (D), 18 h (E) and 21 h (F). (Images courtesy of Dr. Bradley Smith of University of Notre Dame)
**PSVue® Product List**

<table>
<thead>
<tr>
<th>Catalog Number</th>
<th>Name</th>
<th>Structure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-1001</td>
<td>PSVue®794</td>
<td></td>
<td>The PSVue 794 (formerly PSS-794) reagent kit contains components to provide ~0.68 mL of a 1 mM solution of PSVue 794 in aqueous solution. The compound exhibits absorbance and fluorescence excitation maximum at 794 nm and emission maximum at 810 nm. The labeling vehicle provided with the kit (Diluent X) is designed to maximize dye solubility and is suitable for in vitro and in vivo use.</td>
</tr>
<tr>
<td>P-1003</td>
<td>PSVue®480</td>
<td></td>
<td>The PSVue 480 (formerly PSS-480) reagent kit contains components to provide ~0.5 mL of a 1 mM solution of PSVue 480. The compound has an absorbance max at 480 nm and an fluorescence emission max at 519 nm.</td>
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<tr>
<td>P-1004</td>
<td>PSVue®Biotin</td>
<td></td>
<td>Vial contains 1mg of solid. PSVue biotin can be complexed with streptavidin-coated quantum dots (not provided) for in vivo and in vitro use. Procedures to formulate PSVue biotin and prepare the PSVue biotin-streptavidin-coated quantum dot complex are provided.</td>
</tr>
<tr>
<td>P-1005</td>
<td>PSvue®550</td>
<td></td>
<td>The PSVue 550 reagent kit contains components to provide ~0.5 mL of a 1 mM solution of PSVue 550. The compound has an absorbance max at 553 nm and an fluorescence emission max at 615 nm.</td>
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<tr>
<td>P-1006</td>
<td>PSVue®643</td>
<td></td>
<td>The PSVue 643 kit contains 0.25mL of a 1mM solution of PSVue 643 in water. The compound has an absorbance max at 643nm and a fluorescence emission max at 658nm.</td>
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<tr>
<td>P-1007</td>
<td>PSVue®794-Control</td>
<td></td>
<td>This probe contains the same fluorophore present in PSVue 794 but without the Zn-DPA targeting moiety attached. The kit contains 0.6mL of a 1 mM solution of 794-control probe in aqueous solution. The compound exhibits absorbance and fluorescence excitation maximum at 787 nm and emission maximum at 808 nm.</td>
</tr>
<tr>
<td>P-1009</td>
<td>PSVue® 499-WS (mSEEK) Optical Probe</td>
<td></td>
<td>PSVue499-WS, also known as mSEEK, is a water soluble microbial targeted fluorescent imaging agent comprising a Zn-DPA unit and a BODIPY dye.</td>
</tr>
<tr>
<td>P-1010</td>
<td>Propidium Iodide</td>
<td></td>
<td>Propidium Iodide 2mL: (1mg/mL in H2O).</td>
</tr>
</tbody>
</table>

**References:**

- Ayesa U, Gray BD, Pak KY, Chong PL (2016) Liposomes Containing Lipid-Soluble Zn (II)-Bis-dipicolylamine Derivatives Show Potential to be targeted to Phosphatidylserine on the surface of Cancer cells. Mol. Pharmaceut. DOI: 10.1021/acs.molpharmaceut.6b00760.

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**Company Profile**

Molecular Targeting Technologies, Inc. is a privately held U.S.-based Biotechnology Company developing novel medical imaging products.

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