Novel Anesthetics Reduce Side Effects and Facilitate Parenteral Formulation

**Background:** Short acting intravenous anesthetics are used for induction and maintenance of surgical anesthesia as well as for moderate to deep sedation during non-surgical procedures (e.g. colonoscopy and bronchoscopy). The market for such anesthetics is dominated by the generic drug propofol (Diprivan) because of its favorable properties (rapid onset, absence of nausea, and a rapid and pleasant recovery). However, serious side effects include apnea and reduced breathing; and its complex and time-consuming production has led to critical shortages. Moreover, numerous studies have questioned the safety of anesthetics on the developing brain given that many data support anesthetic neurotoxicity in infants. The anesthetic neurosteroids developed by scientists at Washington University in St. Louis offer a promising alternative and provide new clinical and commercial opportunities.

**Technology Description:** A team led by Dr. Covey developed a range of novel steroid anesthetic agents. Like propofol, these novel neurosteroids enhance the actions of GABA (gamma-aminobutyric acid) at GABA$_A$-receptors, one of the most important target sites for general anesthetics. Animal studies have shown desirable anesthetic properties by a rapid onset and duration of anesthesia in rat, followed by a rapid recovery. Importantly, studies showed selected compounds to be non-neurotoxic to newborn rats creating opportunities for a safer alternative for infants and young children. Besides use as anesthetics, these compounds are expected to have potential as anxiolytics, analgesics, anticonvulsants, sleep enhancers, and antidepressants. Moreover, their reduced lipophilicity improves water solubility to facilitate parenteral formulation.

**Key Advantages:**
- Novel composition with greater potency than known neurosteroids
- Includes non-neurotoxic neurosteroids for potential application in infants and young children
- Limited or no disruption of natural neurosteroid production and degradation anticipated
- Straight-forward synthesis with potential for structural modification
- Enhanced water solubility to facilitate parenteral formulation
- Potential as anxiolytics, analgesics, anticonvulsants, sleep enhancers, and antidepressants

**Patents:**
- Issued: 9,365,502; 9,512,170; 9,562,026; and; 9,765,110
- Pending: 14/767,235; EP2956466; 15/333,921; 15/376,938; and 15/157,152

**Publications:** A comprehensive list of Dr. Covey’s work on neurosteroids can be found on PubMed.

**Lead Inventor:** Douglas F. Covey, Ph.D. Professor at the Departments of Developmental Biology and Biochemistry, Washington University in St. Louis School of Medicine.

For over 20 years Dr. Covey has been recognized as an internationally leader in steroid synthesis with a focus on novel neurosteroid analogues as lead compounds for clinical drug development.