SUMMARY ~~OF THE INVENTION~~

The present ~~invention~~disclosure is directed to a buprenorphine sustained release delivery system capable of delivering buprenorphine, a metabolite, or a prodrug thereof for a duration of about 14 days to about 3 months. The buprenorphine sustained release delivery system includes a flowable composition and a solid implant for the sustained release of buprenorphine, a metabolite, or a prodrug thereof. The implant is produced from the flowable composition. The buprenorphine sustained release delivery system provides *in situ* 1-month and 3-month release profiles characterized by an exceptionally high bioavailability and minimal risk of permanent tissue damage and typically no risk of muscle necrosis.

According to a first aspect, there is provided a flowable composition comprising: (a) at least one biodegradable thermoplastic polymer which is at least substantially insoluble in body fluid; (b) a biocompatible polar aprotic organic liquid which comprises N-methyl-2-pyrrolidone, 2-pyrrolidone, N,N-dimethylformamide, dimethyl sulfoxide, propylene carbonate, caprolactam, triacetin, PEG, or any combination thereof; and, (c) 10 wt% to 20 wt% of buprenorphine in the neutral free-base form or buprenorphine in the form of a pharmaceutically acceptable salt, wherein the flowable composition is injected into the body whereupon it transforms in situ into a solid implant.

According to another aspect, there is provided a method of forming a flowable composition as disclosed in the first aspect for use as a controlled release implant, comprising the step of mixing, in any order: (a) a biodegradable thermoplastic polymer that is at least substantially insoluble in aqueous medium or body fluid; (b) a biocompatible polar aprotic liquid; and (c) buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt, wherein the mixing is performed for a sufficient period of time effective to form the flowable composition for use as a controlled release implant.

According to another aspect, there is provided a kit suitable for forming a composition as disclosed in the first aspect, the kit comprising: (a) a first syringe comprising a composition comprising a biodegradable thermoplastic polymer that is at least substantially

insoluble in a body fluid and a biocompatible polar aprotic liquid; and (b) a second syringe comprising buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt; wherein the syringes can be directly connected to each other.

According to another aspect, there is provided a kit suitable for forming a composition as disclosed in the first aspect, the kit comprising a single syringe comprising a composition comprising a biodegradable thermoplastic polymer that is at least substantially insoluble in a body fluid, a biocompatible polar aprotic liquid and buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt.

According to another aspect, there is provided use of an effective amount of buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt in combination with an at least substantially water-insoluble biodegradable thermoplastic polymer and a biocompatible, polar, aprotic organic liquid for the preparation of a medicament to provide the composition as disclosed herein to form a biodegradable implant for the treatment of a medical condition.

In one embodiment, a buprenorphine sustained release delivery system is provided. This delivery system includes a flowable composition and a controlled, sustained release implant. The flowable composition according to this embodiment comprises a biodegradable thermoplastic polymer, a biocompatible, polar organic liquid, and buprenorphine, a metabolite, or a prodrug thereof. The flowable composition may be transformed into the implant by contact with water, body fluid, or other aqueous medium. In one embodiment, the flowable composition is injected into the body whereupon it transforms *in situ* into athe solid implant.

According to a first embodiment of the present ~~invention~~disclosure, therefore, there is provided an injectable flowable composition comprising:

(a) at least one biodegradable thermoplastic polymer which is at least substantially insoluble in body fluid;

(b) a biocompatible polar aprotic organic liquid which comprises an amide, an ester, a carbonate, a lactam, an ether, a sulfonyl, or any combination thereof; which has a

solubility in aqueous medium or body fluid ranging from insoluble to completely soluble in all proportions; and,

(c) 1 wt% to 10wt% of buprenorphine, a metabolite, or a prodrug thereof; wherein the composition is transformed *in situ* into a solid implant by contact with water, body fluid or other aqueous medium.