Never before has a chemotherapy substance been combined with a chemosensitizing agent in the same delivery system. Immix Biopharma has developed a family of micellar nanoparticles that combine a low-dose chemotherapy agent (doxorubicin, DOX, paclitaxel PCL, etc.) with a multi-modal agent, (curcumin, CUR), known to block multiple chemoresistance mechanisms and activate apoptosis in cancer cells. In in-vitro and in-vivo models, this approach has been shown to be a significant inhibitor of NF-kB and other pro-inflammatory proteins with minimal toxicity. Curcumin was selected for use as the most potent NF-kB inhibitor compared with 19 analogues.

Prior to Immix, the major challenge has been the poor water solubility and bioavailability of curcumin. Clinical trials at MD Anderson Cancer Center using this agent in pancreatic cancer patients progressed up to Phase II with hints of efficacy, yet concentrations in plasma were too low to be strongly effective (Kanai M, Yoshimura K, Asada M, et al. A phase I/II study of gemcitabine-based chemotherapy plus curcumin for patients with gemcitabine-resistant pancreatic cancer. Cancer Chemother Pharmacol. 2011 http://www.ncbi.nlm.nih.gov/pubmed/20859741).

Through the unique experience of its co-founder in nanomedicine and drug delivery, Immix overcame this solubility problem by enclosing CUR in a water-soluble nano-carrier that can be administered intravenously. By adding DOX to this nano-carrier, Imx-110 was produced. To date, Immix has completed a toxicology study in guinea pigs with excellent safety of Imx-110. Specifically, no adverse effects were seen in a dose escalation study and the maximal tolerated repeat dose was 4 times greater than the planned therapeutically effective dose. The scalable manufacturing process appropriate for human clinical trials has been developed. HPLC drug detection assay has also been developed.

The second compound, Imx-111, was produced by attaching a tumor-targeting antibody fragment to the surface of the Imx-110 micelle. This targeting antibody fragment (scFv) has an ability to deliver the enclosed cargo to tumor cells that overexpress the target protein on their cell membrane. The biomarker we've chosen to target (Glucose transporter 1; Glut1) provides tumors with the increased glucose uptake required to maintain cancers' viability in terms of energy needs and cellular building blocks (known as the Warburg effect). GLUT1 is widely expressed on a variety of cancers, including breast, colon, pancreas, ovary and many others (http://www.ncbi.nlm.nih.gov/pubmed/15389572).

Therefore, Immix achieves drug-loaded micelle uptake by tumor cells via humanized antibody fragments against the glucose transporter protein GLUT1.

Imx-111 is the first and to date the only, according to open sources, cancer therapeutic in development that addresses and overcomes every critical requirement for efficient solid tumor therapy: it is small enough (<25 nm) to efficiently penetrate the tumor tissue extracellular matrix; it contains a powerful NF-κB inhibitor (CUR) to overcome cancer apoptosis resistance; and it is targeted by an antibody against a key tumor membrane protein (GLUT1) for efficient tumor cell uptake.

To date, Immix has produced several clones of humanized scFv antibody fragments against GLUT1. scFv fragments are much smaller than the whole antibodies or even the Fab fragments and, therefore, are much less immunogenic allowing for safe repeated clinical use without inducing host antibodies. Their smaller size also improves drug diffusion through the high-pressure environment of a tumor mass.

The approach taken by Immix is unique because it focuses on the suppression of the defective apoptosis present in cancer cells. Immix compounds inhibit the main activator of this mechanism rather than just any *one* out of thousands of the downstream proteins activated by NFkB. In such a way, the entire cascade is blocked and the cancer stem cells are unable to compensate by switching to the use of other proteins. Furthermore, Immix compounds are engineered in order to be safely and effectively delivered to tumor tissues in vivo, using compounds with well-known properties and safety profiles.

The current research project aims to substitute easier to manufacture components in place of the more expensive targeting antibodies, thusly speeding up the timeline to clinical trials and greatly reducing the technical risks of manufacturing development.

The first-in-human trial of Immix' first drug, Imx-110, is scheduled for Q3 of 2017.
The drug candidate produced by the current project will be expected to enter clinical trials in in 2018.