The Fourth Industrial Revolution, 4IR, or Industry 4.0, is the concept of applying and adapting intelligent technology in everyday life. The development of digitization and automation also has a very positive effect on environmentally sustainable development. Innovative technologies, including three-dimensional printing (3DP), can cause a model shift in medicine design, manufacture, and use. Instead of conventional large-scale manufacturing, customized printlets (3DP tablets) with a tailored dose, shape, size, and release characteristics could be produced on-demand. Local manufacturing using 3DP technology may change logistics and drug sales. Moreover, personalized medicine can improve the safety and efficiency of therapy. Selective Laser Sintering (SLS) is a versatile additive manufacturing technique. One of the method's advantages is that it is possible to utilize well-established powder processing methods, e.g., mixing, milling, sieving, etc.

One of the starting points of the project is the quotation from the review by Brighentiet al., Journal of Materials Science 2021, 56, 961-998, *"While the range of sinterable polymeric materials is expanding, it is still limited with respect to traditional manufacturing, mainly because of an insufficient understanding of the complete relationship between raw material, process transformation, and final properties."*. The quotation concerns materials, in the form of powders, for manufacturing technical parts. But this sentence is even more true when considering pharmaceutical formulations, which are intrinsically mixtures of powders. In this case, one has real terra incognita.

The physicochemical properties of the powders meeting the requirements of the SLS technique differ significantly from those of the standard manufacturing (e.g., by powder compression or capsule filling) of solid dosage forms. Published so far, invaluable pioneering studies show the possibility of manufacturing various pharmaceutical dosage forms (i.e., immediate release, orally dispersed, modified release). But there is a very little information about the basic phenomena involved in drug manufacturing by the SLS technology, such as mass transport, phase transitions, and the possibility of components interactions during the sintering process, as well as about the influence of powder properties and printing parameters on functional, properties of the product, i.e., mechanical properties, quality, drug release, drug release mechanisms, etc.

There are several goals of the project. The primary one is to acquire fundamental knowledge on the sintering process of single, raw pharmaceutical constituents and binary powder mixtures into printlets. The next goal is to work out strategies for active substance and excipient matching based on this knowledge regarding their structural, morphological, and physicochemical properties. Another one is to examine the impact of technological operations, such as grinding or spray drying, of individual components and their binary mixtures on the performance of the printlets taking into account their influence on drug release. Finally, it will be shown how this knowledge and strategies can be utilized to manufacture real-life pharmaceutic formulations.

To accomplish the goals, a wide spectrum of techniques will be applied for API, excipients, their binary mixtures, and printlet characterization. They include thermal, diffraction, spectroscopic, and chromatographic techniques such as differential scanning calorimetry and thermogravimetry; X-ray powder diffraction and infrared spectroscopy; high-performance liquid chromatography, and size exclusion chromatography. Imaging modalities, such as magnetic resonance imaging techniques, scanning electron microscopy, and X-ray microtomography, will be applied to assess the structural properties of the manufactured printlets. Imaging techniques will also be used for in situ measurements during incubation in dissolution media, giving spatiotemporal structural and physicochemical characteristics of the "working" product.

An expected final result of the project is a preparation of a small library of powders that can be easily utilized to manufacture well-defined pharmaceutical products using SLS technology.