We will present a new approach to develop a data-driven, learning-based framework for predicting outcomes of physical and biological systems, governed by PDEs, and for discovering hidden physics from noisy data. We will introduce a deep learning approach based on neural networks (NNs) and generative adversarial networks (GANs). We also introduce new NNs that learn functionals and nonlinear operators from functions and corresponding responses for system identification. Unlike other approaches that rely on big data, here we “learn” from small data by exploiting the information provided by the physical conservation laws, which are used to obtain informative priors or regularize the neural networks. We will also make connections between Gauss Process Regression and NNs and discuss the new powerful concept of meta-learning. We will demonstrate the power of PINNs for several inverse problems in fluid mechanics, solid mechanics and biomedicine including wake flows, shock tube problems, material characterization, brain aneurysms, etc, where traditional methods fail due to lack of boundary and initial conditions or material properties. We also introduce a new NN, DeepM&Mnet, which uses DeepOnets as building blocks for multiphysics problems, and we will demonstrate its unique capability in a 7-field hypersonics application.