Here we will introduce OpenFIBSEM, a universal API to control Focused Ion Beam Scanning Electron Microscopes (FIBSEM). OpenFIBSEM aims to improve the programmability and automation of electron microscopy workflows in structural biology research. The API is designed to be cross-platform, composable, and extendable. It allows users to use as much or as little of OpenFIBSEM as they choose and integrate it with other software tools. The package provides core functionality such as imaging, movement, milling, and manipulator control, as well as system calibration, alignment, and image analysis modules. Further, a library of reusable user interface components integrated with napari is provided, ensuring easy and efficient application development. OpenFIBSEM currently supports ThermoFisher and TESCAN hardware, with support for other manufacturers planned. To demonstrate the improved automation capabilities enabled by OpenFIBSEM, several example applications compatible with multiple hardware manufacturers are discussed. We argue that OpenFIBSEM provides the foundation for a cross-platform operating system and development ecosystem for FIBSEM systems. The API and applications are open-source and available on GitHub (https://github.com/DeMarcoLab/fibsem).