Griffiths' last formula in section 12.2.1 says $E^2 = p^2 c^2 + m^2 c^4$. When is that valid?

Only for photons Only for massive point like particles, and NOT for photons For massive point like particles AND/OR photons For ALL situations, including complex "systems" that include particles and EM radiation.

Not sure/none of the above/something else

Wait, I'm confused. I thought $E = mc^2?!$ That's not the same as the above equation (If $E=mc^2$ then squaring it gives $E^2 = m^2 c^4$, it's totally missing that whole $p^2 c^2$ term) What's the deal, which is correct, or what's the difference?