Graphical conclusion

Better understanding ES biology/preclinical model

International trials

1st relapse Multiple relapses Phase-II trial Phase-II trial Phase-I/II trial Children/Adult Adolescent/Adult Adolescent/ Adult Mesurable/evaluable disease Mesurable/evaluable disease, Mesurable/evaluable disease, and MRD and MRD Randomised Randomised Single arm CT vs CT + new TTTNew TTT Single / combo New TTT vs (placebo or CT or combo) +/- cross over CT vs combination Basket-trial with Stratified analysis bulky Stratified analysis bulky « sarcomas » and/or disease /MRD disease /MRD « adolescents » cohorts Improve survival Proof of efficacy Tolerance Composite criterion: Composite criterion: First signals of efficacy PFS and RR PFS and RR RR

<u>Figure S4:</u> Graphical conclusion and proposals for future phase-I/II trials enrolling ES recurrent or refractory patients. CT: Chemotherapy, MRD: minimal residual disease, TTT: treatment, Combo: combination.