Published studies of FDA approved drugs against Ebola

1. Madrid PB, Chopra S, Manger ID, Gilfillan L, Keepers TR, Shurtleff AC, Green CE, Iyer LV, Dilks HH, Davey RA, Kolokoltsov AA, Carrion R Jr, Patterson JL, Bavari S, Panchal RG, Warren TK, Wells JB, Moos WH, Burke RL, Tanga MJ**. A systematic screen of FDA-approved drugs for inhibitors of biological threat agents.** PLoS One. 2013;8(4):e60579. doi: 10.1371/journal.pone.0060579. Epub 2013 Apr 5.

In vitro activity in viral pseudotype entry assay for 25 compounds (also activity for live virus replication assay are in bold) :
Amlodipine
Amodiaquine
Biperiden
Carprofen
Chloroquine
Dexbrompheniramine
Dibucaine
Diphenoxylate
Diphenylpyraline
Dipivefrin
Dirithromycin
Erythromycin
Estradiol
Fluoxetine
Hydroxychloroquine
Ketotifen
Levopropoxyphene
Mycophenolate mofetil
Oxyphencyclimine
Paroxetine
Penbutolol
Prochlorperazine
Protriptyline
Toremifene
Trihexyphenidyl

In vivo efficacy data –mouse survivors:
Amlodipine 1/10
Chloroquine 8/10
Dirithromycin 0/10
Erythromycin ethylsuccinate 2/10
Fluoxentine 1/10
Penbutolol 1/10
Prochlorperazine 0/10

2. Johansen LM, Brannan JM, Delos SE, Shoemaker CJ, Stossel A, Lear C, Hoffstrom BG, Dewald LE, Schornberg KL, Scully C, Lehár J, Hensley LE, White JM, Olinger GG. **FDA-approved selective estrogen**

receptor modulators inhibit Ebola virus infection. Sci Transl Med. 2013 Jun 19;5(190):190ra79. doi: 10.1126/scitranslmed.3005471

Clomiphene and Toremifene - Demonstrated *In vitro* activity with live virus; In vivo - protected 9/10 and 5/10 mice respectively

3. Kouznetsova J, Sun W, Martínez-Romero C, Tawa G, Shinn P, Chen CZ, Schimmer A, Sanderson P, McKew JC, Zheng W, García-Sastre A. **Identification of 53 compounds that block Ebola virus-like particle entry via a repurposing screen of approved drugs.** Emerg Microbes Infect. 2014 Dec;3(12):e84. doi: 10.1038/emi.2014.88. Epub 2014 Dec 17.

In vitro activity in Ebola VLP entry assay for 53 compounds:
Vinblastine
Vinorelbine/Navelbine
Vincristine
Colchicine
Nocodazole
Toremifene
Tamoxifen
Digoxin
Clemastine
Raloxifene/Evista
Sunitinib
Thiothixene
Dronedarone
Maprotiline
Daunomycin
Benztropine
Azithromycin
Mebendazole
Trifluoperazine
Clarithromycin
Albendazole
Clomipramine
Propafenone
Carfilzomib
Deslanoside
Maduramicin
Cepharanthine
Clomiphene
Oxibendazole
Daunorubicin
Niclosamide
Zoloft{ (sertraline)
Mefloquine
Tilorone
Bazedoxifene

Topotecan
Bosutinib
Thioproperazine
Spiramycin
Mibefradil
Amodiaquine
Nitrovin
Bifemelane
Bitolterol
Proglumetacin
Aprindine
Cyclomethycaine
Posaconazole
Alverine Citrate
Azaclorzine
Salmeterol
Piperacetazine
Gefitinib
Imipramine
Chloroquine
Nilotinib

Additional 95 active compounds with either moderate activity or without FDA approval for human use
Tazobactam*
Pivoxil Sulbactam*
Dipyrithione
Triparanol
Malachite Green Chloride
Methylbenzethonium Chloride
Perhexiline
Mequitazine
Perphenazine
(S)-(+)-Niguldipine Hydrochloride
Amindocate
Ebastine
Mk-2206
Bepridil
Fluspirilene
Proadifen Hydrochloride
Thioridazine..Hcl
Nitromersol
Clocapramine
Difeterol
Pamicogrel
Fluoperazine Dihydrochloride
Oxethazaine
Fendiline
Rimcazole Dihydrochloride

Indocate
Astemizole
Ftormetazine
Sertindole
Vanoxeamine
Octoclothepin Maleate Salt
Desloratadine
Cinacalcet Hydrochloride
Odanacatib
L-Alpha-Acetyl-N-Normethadol
Lidoflazine
Methiothepin Maleate
Duloxetine Hydrochloride
Tandutinib
Metixene Hydrochloride
Triflupromazine Hydrochloride
Drofenine Hydrochloride
Thenalidine
Mosapramine
Buprenorphine
Pimozide
Prochlorperazine
Homochlorcyclizine..2Hcl
Carbetapentane Citrate
Lapatinib
Zanapezil Fumerate
Rescimetol
Bamipine
Nebivolol Hydrochloride
Proscillaridin A
Chlorprothixene Hydrochloride
Protryptyline Hydrochloride
Metergoline
Propiverine Hydrochloride
Amoxapine
Benzydamine Hydrochloride
Dimethisoquin Hydrochloride
Tioconazole
Sarpogrelate
Halofantrine
Monatepil
Methadone Hydrochloride
Amitriptyline Hydrochloride
Promazine Hydrochloride
Trimipramine Maleate
Pimethixene Maleate
(S)-(+)-Dimethindene Maleate
Cantharidin

Roxindole Hydrochloride
Canertinib
Dopexamine
Butriptyline
Cyproheptadine Hydrochloride
Trihexyphenidyl Hydrochloride
Diphenidol Hydrochloride
Carvedilol
Orphenadrine Hydrochloride
Diphenylpyraline Hydrochloride
Bromperidol
Ami-193
Mesoridazine Besylate
Ipenoxazone Hydrochloride
Dibucaine Hydrochloride
Tomoxetine Hydrochloride
Dasatinib
Premethadone
Sulconazole Nitrate
Octylonium Bromide
Axitinib

4. Gehring G, Rohrmann K, Atenchong N, Mittler E, Becker S, Dahlmann F, Pöhlmann S, Vondran FW, David S, Manns MP, Ciesek S, von Hahn T. **The clinically approved drugs amiodarone, dronedarone and verapamil inhibit filovirus cell entry.** J Antimicrob Chemother. 2014 Aug;69(8):2123-31. doi: 10.1093/jac/dku091. Epub 2014 Apr 7

In vitro activity in GP-pseudovirion entry assay :
Amiodarone

Low or no *in vitro* activity in GP-pseudovirion entry assay:
epigallocatechin-3-gallate (EGCG)
artesunate
cyclosporine A
erlotinib
fingolimod
imatinib,
rapamycin
sorafenib
sotrastaurin
sunitinib
verapamil
bevacizumab
haloperidol
theophylline

In vitro activity against live Ebola virus:

Amiodarone
Dronedarone
Verapamil

Low or no *in vitro* activity against live Ebola virus:
lidocaine
ethosuximide
metoprolol
sotalol

5. Johansen LM, DeWald LE, Shoemaker CJ, Hoffstrom BG, Lear-Rooney CM, Stossel A, Nelson E, Delos SE, Simmons JA, Grenier JM, Pierce LT, Pajouhesh H, Lehár J, Hensley LE, Glass PJ, White JM, Olinger GG. **A screen of approved drugs and molecular probes identifies therapeutics with anti-Ebola virus activity.** Sci Transl Med. 2015 Jun 3;7(290):290ra89. doi: 10.1126/scitranslmed.aaa5597.

In vitro activity for 2635 compounds against live Ebola virus available in supplemental Table S1

In vitro activity demonstrated against live Ebola virus
Aripiprazole
Astemizole
Atovaquone
Azacitidine
Benztropine
Bepridil
Clemastine
Clomiphene
Clomipramine
Dasatinib
Efavirenz
Flupentixol
Fluphenazine
Hycanthone
Lomerizine
Maprotiline
Mycophenolate mofetil
Paroxetine
Pimozide
Piperacetazine
Prochlorperazine
Quinacrine
Sertraline
Simvastatin
Strophanthin
Teicoplanin
Terconazole
Thioridazine
Toremifene

Vinorelbine

Efficacy in Ebola infected mice:
Clomipramine 45 mg/kg QD 40%
Lomerizine 22 mg/kg QD 30%
Aripiprazole* 20 mg/kg QD 10%
Teicoplanin 14 mg/kg QD 0%
Paroxetine 15 mg/kg QD 0%
Efavirenz 15 mg/kg QD 0%

6. Falzarano D, Safronetz D, Prescott J, Marzi A, Feldmann F, Feldmann H. **Lack of protection against ebola virus from chloroquine in mice and hamsters.** Emerg Infect Dis. 2015 Jun;21(6):1065-7. doi: 10.3201/eid2106.150176.

Mouse and guinea pigs treated with 90 mg/kg chloroquine demonstrated no survival benefit with ma-Ebola challenge but also drug toxicity.
Guinea pigs treated with a combination of antibiotics that included 50 mg/kg chloroquine showed no toxicity but also no survival benefit with ma-Ebola challenge

7. Sakurai Y, Kolokoltsov AA, Chen CC, Tidwell MW, Bauta WE, Klugbauer N, Grimm C, Wahl-Schott C, Biel M, Davey RA. **Ebola virus. Two-pore channels control Ebola virus host cell entry and are drug targets for disease treatment**. Science. 2015 Feb 27;347(6225):995-8. doi: 10.1126/science.1258758.

In vitro activity demonstrated against live Ebola virus
Verapamil
Tertandrine (not FDA approved)

8. Hensley LE, Dyall J, Olinger GG Jr, Jahrling PB. **Lack of effect of lamivudine on Ebola virus replication.** Emerg Infect Dis. 2015 Mar;21(3):550-2

Lamivudine did not have in vitro activity against 2 live Ebola virus variants tested in multiple cell types.

9. Smith LM, Hensley LE, Geisbert TW, Johnson J, Stossel A, Honko A, Yen JY, Geisbert J, Paragas J, Fritz E, Olinger G, Young HA, Rubins KH, Karp CL. **Interferon-β therapy prolongs survival in rhesus macaque models of Ebola and Marburg hemorrhagic fever.** J Infect Dis. 2013 Jul 15;208(2):310-8

In this study, early postexposure treatment with IFN-β significantly increased survival time of rhesus macaques infected with a lethal dose of Ebola virus, although it failed to alter mortality.