Supplementary information

Drug repurposing/repositioning as a therapeutic strategy against *Streptococcus pneumoniae*: cell membrane as potential target

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Figure S1

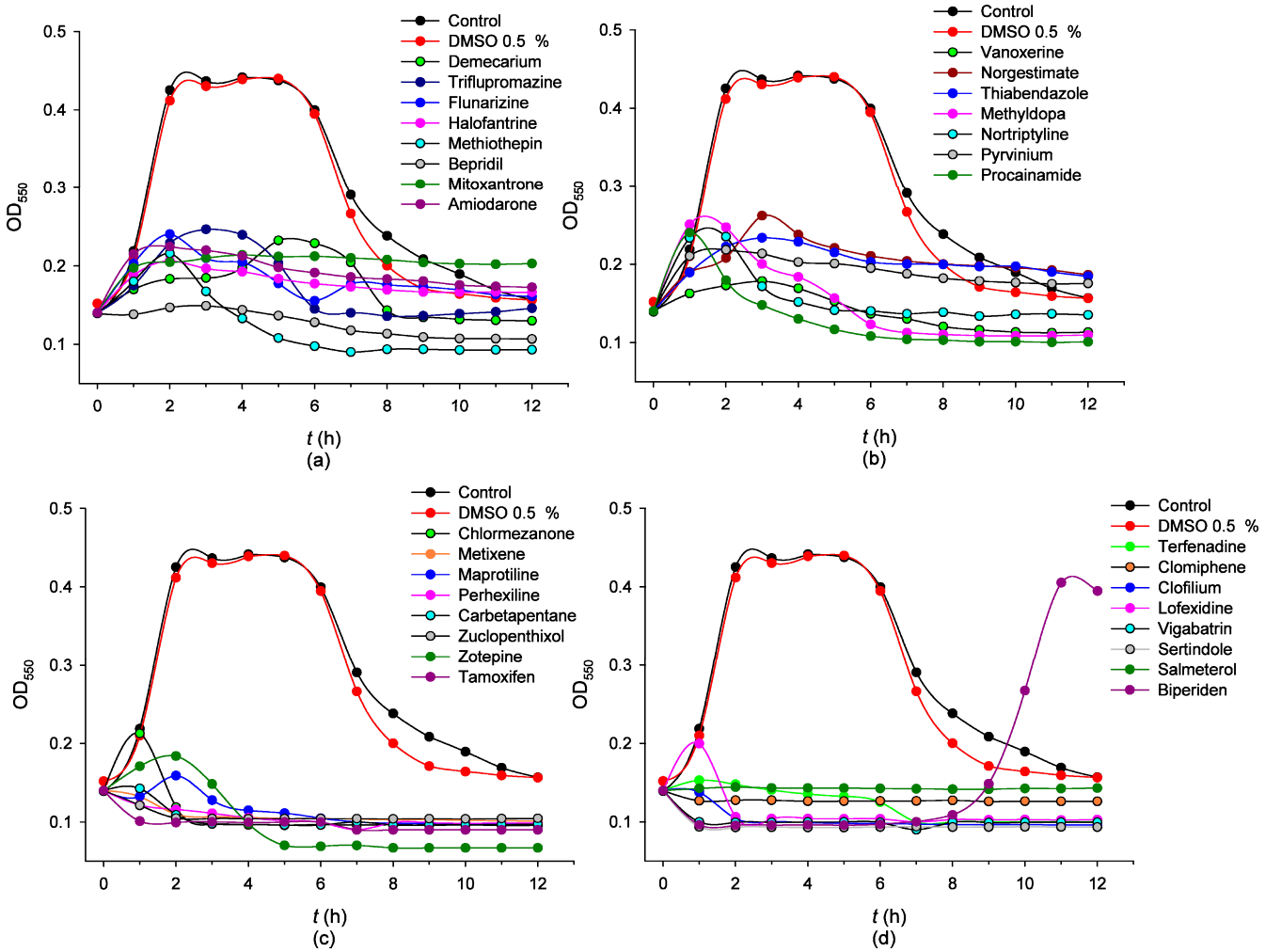


Figure S1. (a-d) Planktonic cultures of *S. pneumoniae* R6CIB17 in the presence of 50 µM concentration of the 31 primary selected molecules (red circles in Figure 1a of the main text). Each compound was added at the early exponential phase.

Table S1

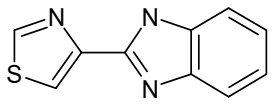
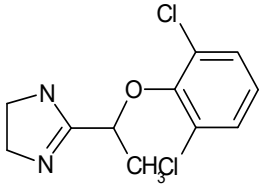
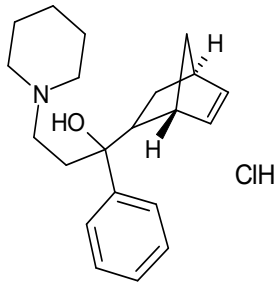
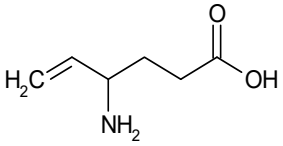
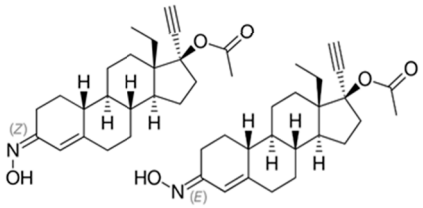
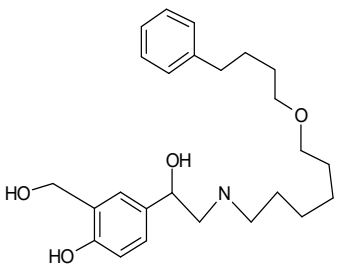
Compound	CAS ID	Chemical structure	Therapeutic approved use	Mechanism of action
1 Thiabendazole	148-79-8		Anthelmintic	Microtubule inhibitor
2 Lofexidine	31036-80-3		Opinoid withdrawal symptoms, antihypertensive	Alpha2-adrenergic receptor agonist
3 Biperiden hydrochloride	1235-82-1		Antiparkinsonian	Anticholinergic
4 Vigabatrin	60643-86-9		Anticonvulsant GABA	Transaminase inhibitor
5 Norgestimate	35189-28-7		Hormonal contraception Menopausal hormone therapy	Progestogen
6 Salmeterol	89365-50-4		Bronchodilator	Beta 2 adrenergic agonist

Table S1 (cont)

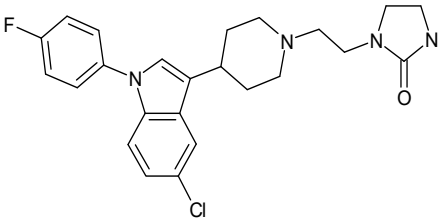
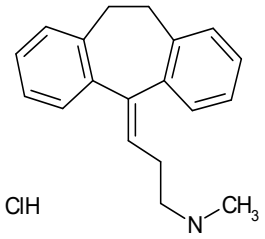
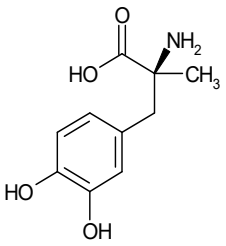
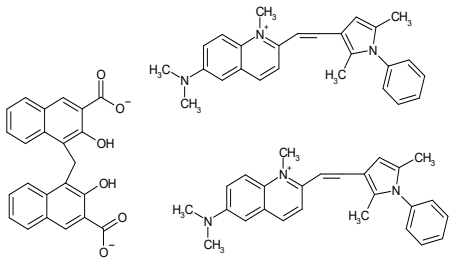
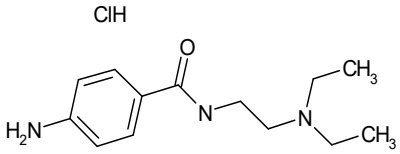
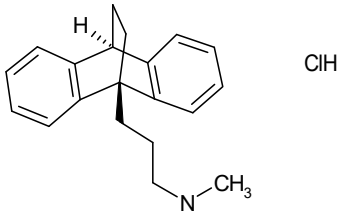
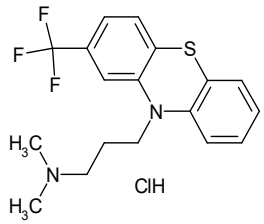
7 Sertindole	106516-24-9		Antipsychotic	Dopamine D2/Serotonin 5-HT2 receptor antagonist
8 Nortriptyline hydrochloride	894-71-3		Antidepressant Sedative Analgesic Muscle relaxant	Norepinephrine uptake inhibitor
9 Methyldopa (L,-)	555-30-6		Antihypertensor	L-aromatic aminoacid decarboxylase inhibitor
10 Pyrvinium pamoate	3546-41-6		Antiparasitic	Metabolic inhibitor
11 Procainamide hydrochloride	614-39-1		Antiarrhythmic Vasodilatator	Alpha antagonist Antinuclear antibodies Anticholinergic
12 Maprotiline hydrochloride	10347-81-6		Antidepressant Sedative Antihistaminic Anxiolytic	Noradrenaline uptake inhibitor 5-HT uptake inhibitor
13 Triflupromazine hydrochloride	1098-60-8		Antipsychotic Tranquilizer Antiemetic Antihypertensor	Dopaminergic antagonist

Table S1 (cont)

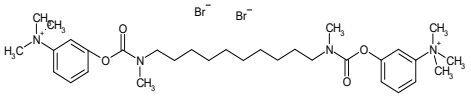
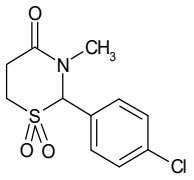
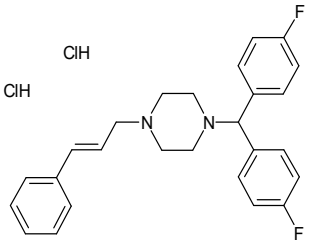
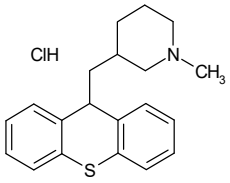
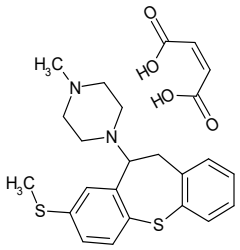
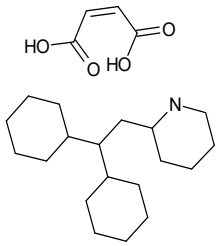
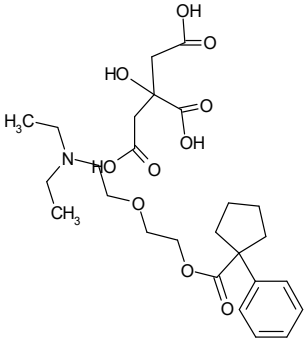
14 Demecarium bromide	56-94-0		Cholinergic (ophtalmic)	Acetyl-cholinesterase inhibitor (parasympathomimetic, cholinomimetic drug or cholinergic receptor stimulating agent)
15 Chlormezanone	80-77-3		Skeletal muscle relaxant	Potentiator of GABA effects
16 Flunarizine dihydrochloride	30484-77-6		Vasodilatator Anticonvulsant Antiarrhythmic	Na^+ channel blocker Ca^{2+} antagonist H1 antagonist
17 Metixene hydrochloride	1553-34-0		Antiparkinsonian	Anticholinergic
18 Methiothepin maleate	19728-88-2		Antipsychotic	5-HT autoreceptor antagonist 5-HT1c antagonist 5-HT release inhibitor electrical or K^+ induced
19 Perhexiline maleate	6724-53-4		Vasodilatator	Ca^{2+} blocking agent
20 Carbetapentane citrate	23142-01-0		Antitussive Spasmolytic	Sigma 1 receptor ligand

Table S1 (cont)

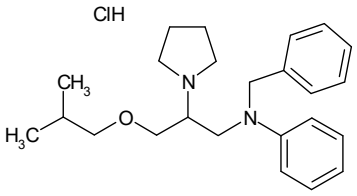
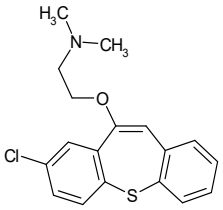
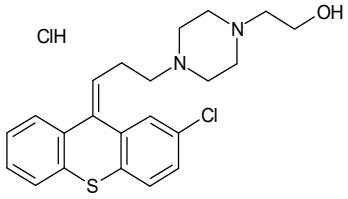
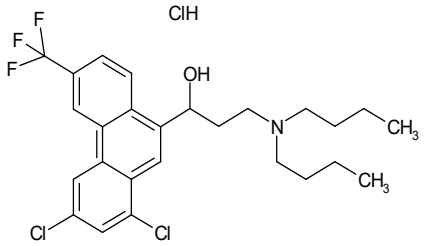
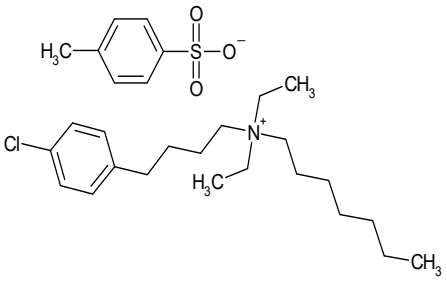
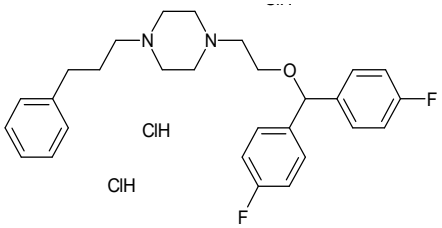
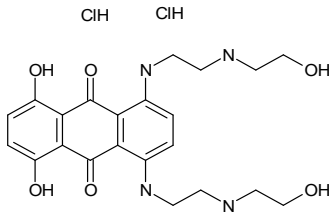
21 Bepridil hydrochloride	74764-40-2		Antianginal	Ca^{2+} channel blocker
22 Zotepine	26615-21-4		antipsychotic	Dopamine D2/serotonin 5-HT2 antagonist
23 Zuclopenthixol hydrochloride	633-59-0		Delirium Schizophrenia Antipsychotic Sedative Neuroleptic Schizophrenia	Dopaminergic receptor antagonist
24 Halofantrine hydrochloride	36167-63-2		Antimalarial	Blocker of HERG channels
25 **Clofilium tosylate**	92953-10-1		Antiarrhythmic	K^+ channel blocker
26 **Vanoxerine (GBR 12909 dihydrochloride)**	67469-78-7		Antidepressant Antiarrhythmic	Dopamine reuptake inhibitor Na^+ channel blocker K^+ channel blocker
27 **Mitoxantrone dihydrochloride**	70476-82-3		Antineoplastic Anticancer	DNA topoisomerase II inhibitor

Table S1 (cont)

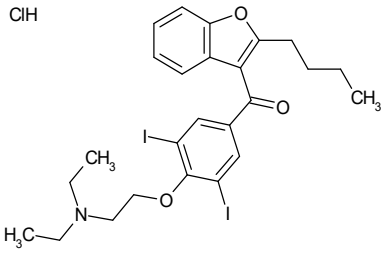
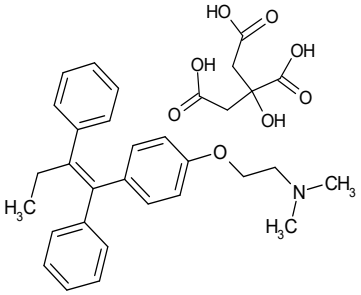
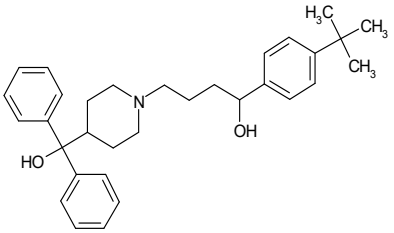
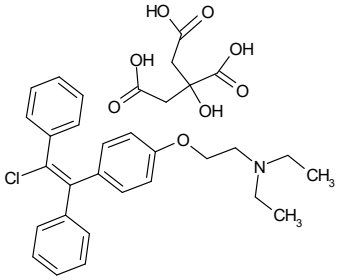
28 Amiodarone hydrochloride	19774-82-4		Antiarrhythmic Antianginal	Na^+ and K* channel blocker; Non-competitive beta-adrenergic blocker
29 Tamoxifen citrate	54965-24-1		Anticancer	Protein kinase C inhibitor Oestrogen receptor antagonist
30 Terfenadine	50679-08-8		Antihistaminic	H1 antagonist Na^+, K^+ and Ca^{2+} channels blocker
31 Clomiphene citrate (Z, E)	50-41-9		Ovulation inductor	Antioestrogen Gonad-stimulating agent

Table S1. Characteristics of the 31 compounds selected as appreciably affecting planktonic pneumococcal growth at 50 μM and that had not been previously reported as antipneumococcal agents (red circles in Figure 1a of the main text). Those that, additionally, induced at 25 μM a decrease in bacterial viability higher than 90 % relative to the control, are represented in bold (compounds 25-31).