CFTR Mutations Eligible for Phase 3 Study of Investigational VX-445 Triple Combination in People with One *F508del* Mutation and One Minimal Function Mutation

The below list includes currently eligible minimal function mutations for the VX-445-102 study as of April 2018 (protocol version 2.0):

CFTR Mutations Eligible for VX17-445-102

MF Mutation Category	Mutation				
Nonsense mutations	Q2X	L218X	Q525X	R792X	E1104X
	S4X	Q220X	G542X	E822X	W1145X
	W19X	Y275X	G550X	W882X	R1158X
	G27X	C276X	Q552X	W846X	R1162X
	Q39X	Q290X	R553X	Y849X	S1196X
	W57X	G330X	E585X	R851X	W1204X
	E60X	W401X	G673X	Q890X	L1254X
	R75X	Q414X	Q685X	S912X	S1255X
	L88X	S434X	R709X	Y913X	W1282X
	E92X	S466X	K710X	Q1042X	Q1313X
	Q98X	S489X	Q715X	W1089X	Q1330X
	Y122X	Q493X	L732X	Y1092X	E1371X
	E193X	W496X	R764X	W1098X	Q1382X
	W216X	C524X	R785X	R1102X	Q1411X
Canonical splice mutations	185+1G→T	711+5G→A	1717-8G→A	2622+1G→A	3121-1G→A
	296+1G→A	712-1G→T	1717-1G→A	2790-1G→C	3500-2A→G
	296+1G→T	1248+1G→A	1811+1G→C	3040G→C (G970R)	3600+2insT
	405+1G→A	1249-1G→A	1811+1.6kbA→G		3850-1G→A
	405+3A→C	1341+1G→A	1811+1643G→T	3120G→A	4005+1G→A
	406-1G→A	1525-2A→G	1812-1G→A	3120+1G→A	4374+1G→T
	621+1G→T	1525-1G→A	1898+1G→A	3121-2A→G	
	711+1G→T		1898+1G→C		
Small (≤3 nucleotide) insertion/deletion (ins/del) frameshift mutations	182delT	1078delT	1677delTA	2711delT	3737delA
	306insA	1119delA	1782delA	2732insA	3791delC
	306delTAGA	1138insG	1824delA	2869insG	3821delT
	365-366insT	1154insTC	1833delT	2896insAG	3876delA
	394delTT	1161delC	2043delG	2942insT	3878delG
	442delA	1213delT	2143delT	2957delT	3905insT
	444delA	1259insA	2183AA→G [a]	3007delG	4016insT
	457TAT→G	1288insTA	2184delA	3028delA	4021dupT
	541delC	1343delG	2184insA	3171delC	4022insT
	574delA	1471delA	2307insA	3171insC	4040delA
	663delT	1497delGG	2347delG	3271delGG	4279insA
	849delG	1548delG	2585delT	3349insT	4326delTC
	935delA	1609del CA	2594delGT	3659delC	
Non-small (>3 nucleotide) insertion/deletion (ins/del) frameshift mutations	CFTRdele1		CFTRdele16-17b	1461ins4	
	CFTRdele2		CFTRdele17a,17b	1924del7	
	CFTRdele2,3		CFTRdele17a-18	2055del9→A	
	CFTRdele2-4		CFTRdele19	2105-2117del13insAGAAA	
	CFTRdele3-10,14b-16		CFTRdele19-21	2372del8	

CFTR Mutations Eligible for Phase 3 Study of Investigational VX-445 Triple Combination in People with One *F508del* Mutation and One Minimal Function Mutation

The below list includes currently eligible minimal function mutations for the VX-445-102 study as of April 2018 (protocol version 2.0):

CFTR Mutations Eligible for VX17-445-102

MF Mutation Category	Mutation		
	CFTRdele4-7	CFTRdele21	2721del11
	CFTRdele4-11	CFTRdele22-24	2991del32
	CFTR50kbdel	CFTRdele22,23	3121-977_3499+248del2515
	CFTRdup6b-10	124del23bp	3667ins4
	CFTRdele11	602del14	4010del4
	CFTRdele13,14a	852del22	4209TGTT→AA
	CFTRdele14b-17b	991del5	

CFTR Mutations Eligible for Phase 3 Study of Investigational VX-445 Triple Combination in People with One *F508del* Mutation and One Minimal Function Mutation

The below list includes currently eligible minimal function mutations for the VX-445-102 study as of April 2018 (protocol version 2.0):

CFTR Mutations Eligible for VX17-445-102

MF Mutation Category	Mutation			
Missense mutations that • Are not responsive in vitro to TEZ, IVA, or TEZ/IVA **and** • %PI >50% and $SwCl^-$ >86 mmol/L	A46D[b] G85E R347P L467P[b] I507del	V520F A559T[b] R560T R560S A561E	Y569D[b] L1065P R1066C L1077P[b] M1101K	N1303K

CFTR: cystic fibrosis transmembrane conductance regulator; IVA: ivacaftor; SwCl: sweat chloride; TEZ: tezacaftor

Source: CFTR2.org [Internet]. Baltimore (MD): Clinical and functional translation of CFTR. The Clinical and Functional Translation of CFTR (CFTR2), US Cystic Fibrosis Foundation, Johns Hopkins University, the Hospital for Sick Children. Available at: http://www.cftr2.org/. Accessed 15 February 2016.

Notes: %PI: percentage of *F508del-CFTR* heterozygous patients in the CFTR2 patient registry who are pancreatic insufficient; SwCl: mean sweat chloride of *F508del-CFTR* heterozygous patients in the CFTR2 patient registry.

[a] Also known as 2183delAA→G.

[b] Unpublished data.