

P·PIBḡ™ CIP·CfC”C,CHCfCfC P· PjCfCfPeP°CḡPēPSPsPIPēPjPē
CḡPμC†PμPiC,PsCḡP°PjPē.

PμC-ClP»CfC PsPrPSPsCḡP°P·PsPIPsPiPs P·P°ClC,PsClCfPIP°PSPSCfC P±C-P»P°ClC,PēPS
PiCḡPμC,ClPiPsPj 24 PiPsPrPēPS PiCḡPēPiPSC-C†CfC” CḡPsP·PIPēC,PsPe
ClPiCḡPēC†PēPSPμPSPēC... PiC-ClC,P°PjC-PSPsPj CēPeC-CḡPSPēC... CḡPμP°PeC†C-PNē, C%oPs
PiCḡPsCfPIP»CfCḡC,CHCfCfC PiCfC...PēCḡCfPjPē C,P° PiPsC†PμCḡPIPsPSC-PSPSCfCfCj.

Pj PeP»C-PSC-C†PSPēC... PrPsClP»C-PrPμPSPSCfC..., PiCḡPsPIPμPrPμPSPēC... P·P°
CfC†P°ClC,Cḡ PrPsCḡPsClP»PēC... C- PiC-PrP»C-C,PeC-PI P· P°P»PμCḡPiC-C†PSPēPj
CḡPēPSPsPePsPSḡḡ™ CḡPSPeC,PēPIC-C,PsPj (ClPμP·PsPSPSPēPj C- C†C-P»PsCḡC-C†PSPēPj),
PiCḡPēPNēPsPj 20 PjPi P±C-P»P°ClC,PēPSCfC 1 CḡP°P· PSP° PrPsP±CfC PIPiCḡPsPrPsPIPμ 14ḡḡ”28
PrPSC-PI PIPēCfPIPēPICfCfC PμC,,PμPeC,PēPIPSPēPj Cf PiPsP»PμPiCēPμPSPSC- C,P°PePēC...
ClPēPjPiC,PsPjC-PI, ClPe C†C...P°PSPSCfC, PIPēPrC-P»PμPSPSCfC P· PSPsClP°,
ClPIPμCḡP±C-Pμ Cf PSPsClC-, P·P°PeP»P°PrPμPSC-ClC,CH PSPsClP°, ClPIPμCḡP±C-Pμ
PsC†PμPNē, ClP»CHPsP·PsC,PμC†P° C,P° PiPsC†PμCḡPIPsPSC-PSPSCfC PsC†PμPNē.
PŸPēPjPiC,PsPjPē PμC,,PμPeC,PēPIPSPs PePsPSC,CḡPsP»CḡPIP°P»PēClCfC
P±C-P»P°ClC,PēPSPsPj PiCḡPsC,ClPiPsPj 24 PiPsPrPēPS.

Pj PrPIPsC... PeP»C-PSC-C†PSPēC... PrPsClP»C-PrPμPSPSCfC..., PI ClPePēC... P±CḡP°P»Pē
CfC†P°ClC,CH PiP°C†C-C”PSC,Pē P· C...CḡPsPSC-C†PSPsCḡ C-PrC-PsPiP°C,PēC†PSPsCḡ
PeCḡPsPiPēPIBḡ™ CIPSPePsCḡ, P·P°ClC,PsClCfPIP°PSPSCfC 20 PjPi P±C-P»P°ClC,PēPSCfC 1
CḡP°P· PSP° PrPsP±CfC PiCḡPsC,ClPiPsPj 28 PrPSC-PI P±CfP»Ps PμC,,PμPeC,PēPIPSPēPj Cf
PiPsClP»P°P±P»PμPSPSC- C-PSC,PμPSCfPēPIPSPsClC,C- ClPIPμCḡP±PμPμCfC C,P°
P·PjPμPSCēPμPSPSC- PeC-P»CHPePsClC,C- C- CḡPsP·PjC-CḡCfC PiCfC...PēCḡC-PI, P°
C,P°PePsPμ PrPēClPēPsPjC,,PsCḡC,Cf, PIPēPeP»PēPeP°PSPsPiPs PeCḡPsPiPēPIBḡ™ CIPSPePsCḡ.
Pj PiP°C†C-C”PSC,C-PI ClPiPsClC,PμCḡC-PiP°P»PsClCfC PiPsPeCḡP°C%oPμPSPSCfC ClPSCfC
C,P° ClPePsClC,C- PμPēC,C,Cl.

Pj PeP»C-PSC-C†PSPēC... PrPsClP»C-PrPμPSPSCfC... P±C-P»P°ClC,PēPSCfC
PeP»C-PSC-C†PSPs P·PSP°C†CfC%oPsPiPs PiPsPrPsPIPμPμPSPSCfC C-PSC,PμCḡPIP°P»CfC QTCl
P°P±Ps ClPePsPiPsClCḡ C-PSCēPsPiPs PIPiP»PēPICfC PSP° ClPμCḡC†PμPIPs-ClCfPrPēPSPSCfC
ClPēClC,PμPjCfC PSPμ ClPiPsClC,PμCḡC-PiP°P»PsClCfC, PSP°PIC-C,CH PiCḡPē
P·P°ClC,PsClCfPIP°PSPSC- Cf PrPsP·C- 200 PjPi PSP° PrPsP±CfC (C%oPs PI 10 CḡP°P·C-PI
PiPμCḡPμPIPēC%oCfC” PeP»C-PSC-C†PSCfC PrPsP·Cf) PiCḡPsC,ClPiPsPj 7 PrPSC-PI Cf 9
CfC†P°ClPSPēPeC-PI P°P±Ps Cf CḡP°P·C- PsPrPSPsC†P°ClPSPsPiPs
P·P°ClC,PsClCfPIP°PSPSCfC P· C-PSPiC-P±C-C,PsCḡP°PjPē P-PiP»C-PePsPiCḡPsC,PμC—PSCfC (P-
gp), C,P°PePēPjPē ClPe PePμC,PsPePsPSP°P·PsP» (24 CfC†P°ClPSPēPePē) C-
PμCḡPēC,CḡPsPjC-C†PēPS (24 CfC†P°ClPSPēPePē). PḡCḡC-Pj C,PsPiPs, P±CfP»Ps
PiCḡPsPIPμPrPμPSPs CḡPμC,PμP»CHPSPμ PrPsClP»C-PrPμPSPSCfC QT P·P°
CfC†P°ClC,Cḡ 30 PrPsP±CḡPsPIPsP»CHC†C-PI.

Pj PePsPSC,CḡPsP»CHPsPIP°PSPēC... PeP»C-PSC-C†PSPēC... PrPsClP»C-PrPμPSPSCfC...
P·P°ClC,PsClCfPIP°PSPSCfC PI CḡPμPePsPjPμPSPPrPsPIP°PSC-PNē PrPsP·C- 20 PjPi 1 CḡP°P· PSP°
PrPsP±CfC PiCḡPsC,,C-P»CH P±PμP·PiPμPePē P±C-P»P°ClC,PēPSCfC C,P° PiP»P°C†PμP±Ps
PIC-PrPSPsClPSPs C†PμPSC,CḡP°P»CHPSPsC— PSPμCḡPIPsPIPsC— ClPēClC,PμPjPē (PiKpŸ)
P±CfP»Pē ClC...PsPμPēPjPē, P° C†P°ClC,PsC,P° PiPsClPIPē ClPsPSP»PēPIPsClC,C- PSP° C,P»C-
PiCḡPēPNēPsPjCfC P±C-P»P°ClC,PēPSCfC ClC,P°C,PēClC,PēC†PSPs PSPμ
PIC-PrCḡC-P·PSCfCfC PIC-Pr C,P°PePsC— PiCḡPē P·P°ClC,PsClCfPIP°PSPSC-
PiP»P°C†PμP±Ps. P’C-P»P°ClC,PēPS Cf PrPsP·P°C... PrPs 40 PjPi PSP° PrPsP±CfC PSPμ
PIPiP»PēPIP°PI PSP° PiClPēC...PsPjPsC,PsCḡPSC- PiPsPeP°P·PSPēPePē Cf PeP»C-PSC-C†PSPēC...

PrPsCfP»C-PrP¶PµPSPSC¶C... C,P° PSP° P·PrP°C,PSC-CfC,CH PePµC¶CfPIP°C,Pë
C,C¶P°PSCfPïPsC¶C,PSPëPjPë P·P°CfPsP±P°PjPë Cí CfC,P°PSPrP°C¶C,PSPsPjCf C,PµCfC,C-
PSP° PIPsPrC-PSPSC¶C.

Pj PïP°C†C-C"psc,C-PI P»C-C,pschbpspïps PIC-PeCf (≥ 65 C¶PspPeC-PI), C¶PeC- P±C¶P°P»Pë
CfC†P°CfC,CH Cí PrPsCfP»C-PrP¶PµPSPSC¶C... II C- III C,,P°P·Pë,
PµC,,PµPeC,PëPIPSC-CfC,CH C- P±PµP·PïPµPeP° PïC¶PµPïP°C¶P°C,Cf PSPµ
PIC-PrC¶C-P·PSC¶C¶P»PëCfC¶C PIC-Pr C,P°PePëC... Cí PïP°C†C-C"psc,C-PI PjPsP»PsPrC¶PsPïPs
PIC-PeCf.

Pj PïC-CfP»C¶C¶PµC"cfC,C¶P°C†C-PN°PSPsPjCf PrPsCfP»C-PrP¶PµPSPSC-,
PïC¶PspPIPµPrPµPSPsPjCf P·P° CfC†P°CfC,C¶ 146 PïP°C†C-C"psc,C-PI P»C-C,pschbpspïps
PIC-PeCf, PI PïPsC¶C-PIPSC¶PSPSC- P·C-PSC¶PëPjPë PrPsC¶PspCfP»PëPjPë
CfC†P°CfPSPëPeP°PjPë PIC-PrPjC-PSPSPscfC,PµPN° PI PïC¶Psc,,C-P»C- P±PµP·PïPµPePë
PIPëC¶PIP»PµPSPs PSPµ P±CfP»Ps.

P"C-C,Pë. PµC-PrP»C-C,PePë (PIC-PePsPj 12B¶"17 C¶PspPeC-PI) P±CfP»Pë
PIPëP»C¶C†PµPSC- PI PïC¶PspPïC¶P°PjCf PeP»C-PSC-C†PSPsC— C¶Psp·C¶Psp±PePë. P—
PSPëC... 128 PsCfC-P± PsC,C¶PëPjCfPIP°P»Pë P±C-P»P°CfC,PëPS PïC-Pr C†P°Cf
PeP»C-PSC-C†PSPëC... PrPsCfP»C-PrP¶PµPSC¶ (81 B¶" PI PïPsPrPIC-PN°PSPs CfP»C-PïPëC...
PrPsCfP»C-PrP¶PµPSPSC¶C... P°P»PµC¶Pic-C†PSPsPïPs
C¶PëPSPsPePsPsb¶™ C¶PSPeC,PëPIC-C,Cf), C¶PµC¶C,P° 116 CfC†P°CfPSPëPeC-PI P±CfP»Pë
C¶P°PSPrPsPjC-P·PsPIP°PSC- PI PïC¶CfPïPë, C¶PeC- PsC,C¶PëPjCfPIP°P»Pë P°PeC,PëPIPSC-
PïC¶PµPïP°C¶P°C,Pë PïPsC¶C-PIPSC¶PSPSC¶C P°P±Ps PïP»P°C†PµP±Ps.
P'C-PrPjC-PSPSPscfC,PµPN° PI PµC,,PµPeC,PëPIPSPscfC,C- C,P° P±PµP·PïPµC†C- PjC-P¶
PrPsC¶PspCfP»PëPjPë C- PïC-PrP»C-C,PeP°PjPë PSPµ CfPïPsCfC,PµC¶C-PïP°P»PscfC¶C.

PαP°C¶PjP°PePsPeC-PSPµC,PëPeP°.

P'CfPjPsPeC,CfPIP°PSPSC¶C. PµC-CfP»C¶C PïPµC¶PspC¶P°P»CHbpspïps
P·P°CfC,PsCfCfPIP°PSPSC¶C P±C-P»P°CfC,PëPS C¶PIPëPrPePs
PICfPjPsPeC,CfC"C,CHCfC¶C, P° PN°PsPïPs PjP°PeCfPëPjP°P»CHbpsp°
PePsPSC†PµPSC,C¶P°C†C-C¶Cf Cí PïP»P°P·PjC- PrPsCfC¶CfPïP°C"C,CHCfC¶C
PïC¶PëP±P»PëP·PSPs C†PµC¶PµP· 1,3 PïPsPrPëPSPë. PkP°PePsPïPëC†PµPSPSC¶C PSPµ
CfPïPsCfC,PµC¶C-PïP°P»PscfC¶C. P¶PµC¶PµPrPSC-PN° PïPsPeP°P·PSPëPe
P±C-PsPrPsCfC,CfPïPSPscfC,C- P±C-P»P°CfC,PëPSCf PïC¶Pë
PïPµC¶PspC¶P°P»CHbpspïpsPjCf P·P°CfC,PsCfCfPIP°PSPSC- CfC,P°PSPsPIPëC,CH 61 %.

P PsP·PïPsPrC-P». P"PsCfP»C-PrP¶PµPSPSC¶C *in vitro* C,P° *in vivo* PïPsPeP°P·P°P»Pë, C%°Ps
P±C-P»P°CfC,PëPS C" CfCfP±CfC,C¶P°C,PsPj Pgp (PrPëPI. C¶Psp·PrC-P»
B«P'P·P°C"PjPsPrC-C¶C P· PePµC,PsPePsPSP°P·PsPj, PµC¶PëC,C¶PspjC-C†PëPSPsPj C,P°
PrPëP»C,C-P°P·PµPjPsPjB») C,P° OATP (PrPëPI. C¶Psp·PrC-P» B«P'P·P°C"PjPsPrC-C¶C P·
PïC¶PµPN°PïC,,C¶CfC,PsPIPëPj CfPsPePsPjB»). P'C-P»P°CfC,PëPS, PsC†PµPIPëPrPSPs, PSPµ C"
CfCfP±CfC,C¶P°C,PsPj PïPµC¶PµPSPscfPSPëPeP° BCRP P°P±Ps PSPëC¶PePsPIPëC...
PïPµC¶PµPSPscfPSPëPeC-PI P¶P¶P¶2, P¶P¶P¶1 C,P° P¶P¶P¶3. P"°PSC-
PrPsCfP»C-PrP¶PµPSC¶ *in vitro* PSPµ PrP°C¶C,CH PïC-PrCfC,P°PI PIPIP°P¶P°C,Pë, C%°Ps PI
CfPëCfC,PµPjPSPsPjCf PeC¶PspIPsC,PsPeCf P±C-P»P°CfC,PëPS PïC¶PëPïPSC-C†CfC"
P°PeC,PëPIPSC-CfC,CH C,P°PePëC... P±C-P»PeC-PI-PïPµC¶PµPSPscfPSPëPeC-PI, C¶Pe P-gp,
MRP2, BCRP, BSEP, OATP1B1, OATP1B3, OATP2B1, OAT1, OAT3, OCT1, OCT2 C,P° NTCP,
PsCfPeC-P»CHPePë PN°PsPïPs P·PrP°C,PSC-CfC,CH C-PSPiC-P±CfPIP°C,Pë P-gp, OATP2B1 C,P°
OCT1 PSPµP·PSP°C†PSP° C- C...P°C¶P°PeC,PµC¶PëP·CfC"C,CHCfC¶C PïPsPeP°P·PSPëPePsPj IC₅₀

≥ 300 PjPeP_н, C%_oPs P·PSP°C±PSPs PīPμC_тPμPIPëC%_oC_тC” C_тPsP·C_тP°C...C_тPSPePsPIPëP_н
PīPsPeP°P·PSPëPe PjP°PeC_тPëPjP°P»C_тHPSPsC— PePsPSC±PμPSC,C_тP°C±C— PI PīP»P°P·PjC—
(C_{max}) C_т C_тP°P·C— PeP»C—PSC—C±PSPsPiPs P·P°C_тC,P_sC_тC_тPIP°PSPSC_т P±C—P»P°C_тC,PëPSC_т.
P_тP°PePëPj C±PëPSPsPj, PīPsPrC—P±PSC— PIP·P°C”PjPsPrC—C— PSPμ PjP°C,PëPjC_тC,C_т
PeP»C—PSC—C±PSPsPiPs P·PSP°C±PμPSPSC_т. PμC_тPsC,Pμ C_тPμP·C_тP»C_тHC,P°C,Pë
P°PSP°P»PsPiC—C±PSPëC... PrPsC_тP»C—PrP_тμPμPSC_т PIPeP°P·C_тC_тC,C_тHPSP° C,Pμ, C%_oPs
C—PSPiC—P±C_тPIP°PSPSC_т P±C—P»P°C_тC,PëPSPsPj P±C—P»PeC—PI—PīPμC_тPμPSPsC_тPIPëPeC—PI,
C%_oPs P·PSP°C...PsPrC_тC,C_тHC_тC_т PI C_тP»PëP·PsPIC—P_н PsP±PsP»PsPSC±C—
PePëCëPμC±PSPëPeC_т (PSP°PīC_тPëPeP»P°Pr P-gp), PIPëPeP»C_тC±PëC,Pë PSPμ PjPsP_тPSP°.
PμC_тPë P·P°C_тC,P_sC_тC_тPIP°PSPSC— C_т C,PμC_тP°PīPμPIC,PëC±PSPëC... PrPsP·P°C... 84B_т”90 %
P±C—P»P°C_тC,PëPSC_т P·PIB_т™ C_тP·C_тC”C,C_тHC_тC_т P· P±C—P»PeP°PjPë PīP»P°P·PjPë
PeC_тPsPIC—.

P’C—PsC,C_тP°PSC_тC,,PsC_тPjP°C±C—C_т. PJ PrPsC_тP»C—PrP_тμPμPSPSC_тC... in vitro
P±C—P»P°C_тC,PëPS PSPμ PIPëC_тPIPëPI P·PrP°C,PSPsC_тC,C— C—PSP_тC_тPeC_тPIP°C,Pë
P°P±Ps PīC_тPëPiPSC—C±C_тPIP°C,Pë P°PeC,PëPIPSC—C_тC,C_т C—P·PsC,,PμC_тPjPμPSC,C—PI
CYP450.

P’PëPIPμPrPμPSPSC_т. PJ PrPsC_тP»C—PrP_тμPμPSPSC— P±P°P»P°PSC_тC_т PjP°C_тPë,
PīC_тPsPIPμPrPμPSPsPiPs P·P° C_тC±P°C_тC,C_т P·PrPsC_тPsPIPëC... PrPsP±C_тPsPIPsP»C_тHC±C—PI,
PīC—C_тP»C_т PsPrPSPsC_тP°P·PsPIPsPiPs P·P°C_тC,P_sC_тC_тPIP°PSPSC_т ¹⁴C—P±C—P»P°C_тC,PëPSC_т
PI PrPsP·C— 20 PjPi PjP°P_нP_тμ 95 % PīC_тPëP_нPSC_тC,P_sC— PrPsP·Pë PIPëC_тPIP»C_тP»PëC_тC_т
PI C_тPμC±C— (28,3 %) C,P° PeP°P»C— (66,5 %) C_т PIPëPiP»C_тPrC— PSPμP·PjC—PSPμPSPsPiPs
P±C—P»P°C_тC,PëPSC_т, P· C±PsPiPs PjPsP_тPSP° P·C_тPsP±PëC,Pë PIPëC_тPSPsPIPsPe, C%_oPs PI
PsC_тPiP°PSC—P·PjC— P»C_тPrPëPSPë P±C—P»P°C_тC,PëPS PjPμC,P°P±PsP»C—P·C_тC”C,C_тHC_тC_т
PSPμP·PSP°C±PSPëPj C±PëPSPsPj. PJ C_тPμC_тPμPrPSC_тPsPjC_т PīPμC_тC—PsPr
PSP°PīC—PIPIPμPrPμPSPSC_т P±C—P»P°C_тC,PëPSC_т C_т P·PrPsC_тPsPIPëC...
PrPsP±C_тPsPIPsP»C_тHC±C—PI C_тC,P°PSPsPIPëC,C_т 14,5 PiPsPr.

P»C—PSC—P_нPSC—C_тC,C_т. PJ PrPsC_тP»C—PrP_тμC_тPIP°PSPsPjC_т PrC—P°PīP°P·PsPSC— PrPsP·
(PIC—Pr 5 PrPs 220 PjPi) P±C—P»P°C_тC,PëPS PIPëC_тPIP»C_тC” P»C—PSC—P_нPSC_т
C,,P°C_тPjP°PePsPeC—PSPμC,PëPeC_т P· PSPëP·C_тPePsC_т PjC—P_тμC_тC_тP±B_т™ C”PeC,PSPsC_т
PIP°C_тC—P°P±PμP»C_тHPSC—C_тC,C_т.

PμPsC_тC_тCëPμPSPSC_т C,,C_тPSPeC±C—C— PSPëC_тPsPe. P”PsC_тP»C—PrP_тμPμPSPSC_т P·P°
C_тC±P°C_тC,C_т PīP°C±C—C”PSC,C—PI P· C_тC—P·PSPëPj C_тC,P°PSPsPj C,,C_тPSPeC±C—C—
PSPëC_тPsPe PīPsPeP°P·P°P»Ps, C%_oPs C_т C_тP°P·C— PSPsC_тPjP°P»C_тHPSPsC—
C,,C_тPSPeC±C—C— PSPëC_тPsPe (CëPIPëPrPeC—C_тC,C_т PeP»C_тP±PsC±PePsPIPsC—
C,,C—P»C_тHC,C_тP°C±C—C— (PëP_тP_т) > 80 PjP»/C...PI/1,73 Pj²) C_тPμC_тPμPrPSC_т AUC_{0B_т—P}
(B± C_тC,P°PSP_тP°C_тC,PSPμ PIC—PrC...PëP»PμPSPSC_т) C_тC,P°PSPsPIPëC,C_т
737,4 (B±260,8) PSPi×PiPsPr/PjP», P·P° PSP°C_тPIPSPsC_тC,C— PīPsC_тC_тCëPμPSC_т
C,,C_тPSPeC±C—C— PSPëC_тPsPe P»PμPiPePsPiPs C_тC,C_тPīPμPSC_т C,C_тP_тμPePsC_тC,C— (PëP_тP_т =
50B_т”80 PjP»/C...PI/1,73 Pj²) C±PμP_н PīPsPeP°P·PSPëPe C_тC,P°PSPsPIPëC,C_т 967,4 (B± 140,2)
PSPi×PiPsPr/PjP», C_т C_тP°P·C— PīPsC_тC_тCëPμPSC_т C_тPμC_тPμPrPSC_тPsPiPs C_тC,C_тPīPμPSC_т
C,C_тP_тμPePsC_тC,C— (PëP_тP_т = 30B_т”<50 PjP»/C...PI/1,73 Pj²) B_т”
1384,2 (B±263,23) PSPi×PiPsPr/PjP», P° C_т C_тP°P·C— PīPsC_тC_тCëPμPSC_т
C,C_тP_тμPePsPiPs C_тC,C_тPīPμPSC_т (PëP_тP_т <30 PjP»/C...PI/ 1,73 Pj²) B_т” 1708,5 (B±
699,0) PSPi×PiPsPr/PjP».

PJ PīP°C±C—C”PSC,C—PI P· PSPsC_тPjP°P»C_тHPSPsC_т C,,C_тPSPeC±C—C”C_тHPSPëC_тPsPe

СГРµСҗРµРrPSC-PM (B± СГC,.. PIC-PrC....) PµСҗC-PsPr PSP°PіC-PIPIPёPIPµPrPµPSPSCII P±C-P»P°СГC,PёPSCr СГC,P°PSPsPIPёPI 9,3 (B± 2,8) PiPsPr, Cr PIP°C+C-C"PSC,C-PI P· PİPsCҗCrCёPµPSPSCII PjPё P»PµPiPePsPiPs СГC,CrPµPµPSCII C,CII P¶PePsСГC,C- Bҗ" B 15,1 (B± 7,7) PiPsPr, Cr PIP°C+C-C"PSC,C-PI P· PİPsCҗCrCёPµPSPSCII PjPё СГРµСҗРµРrPSCII PµPiPs СГC,CrPµPµPSCII C,CII P¶PePsСГC,C- Bҗ" 10,5 (B± 2,3) PiPsPr, P° Cr PIP°C+C-C"PSC,C-PI P· PİPsCҗCrCёPµPSPSCII PjPё C,CII P¶PePsPiPs СГC,CrPµPµPSCII Bҗ" 18,4 (B± 11,4) PiPsPr. PµСҗP°PeC,PёC±PSPs Cr PICГC-C... PIP°C+C-C"PSC,C-PI C±PµСҗРµP· 48Bҗ"72 PiPsPrPёPSPё PіC-СГP»CII PіCҗPёPNёPsPjCr P±C-P»P°СГC,PёPS PI СГРµC±C- PSPµ PIPёCII PIP»CII PICГCII. PµPsPrC-P±PSC- P·PjC-PSPё C,,P°СҗPjP°PePsPeC-PSPµC,PёPePё PSPµ PİPsPIPёPSPSC- PjP°C,Pё PeP»C-PSC-C±PSPsPiPs P·PSP°C±PµPSPSCII C,P° PIPİP»PёPICr PSP° P±PµP·PİPµPeCr P·P°СГC,PsСГCrPIP°PSPSCII P±C-P»P°СГC,PёPSCr, PsСГPeC-P»CҗPePё PNёPsPiPs PePsPSC±PµPSC,CҗP°C+C-C— PI PİP»P°P·PjC- Cr PIP°C+C-C"PSC,C-PI P· PİPsCҗCrCёPµPSPSCII PjPё C,,CrPSPeC+C-C— PSPёCҗPsPe P·P°P»PёCёP°CҗC,CҗCГCII PI P±PµP·PİPµC±PSPёC... PjPµP¶P°C....

PµPsCҗCrCёPµPSPSCII C,,CrPSPeC+C-C— PİPµC±C-PSPePё.

PαP°СҗPjP°PePsPeC-PSPµC,PёC±PSC- PrP°PSC- C%PsPrPs PIP°C+C-C"PSC,C-PI P· PİPsCҗCrCёPµPSPSCII Pj C,,CrPSPeC+C-C— PİPµC±C-PSPePё PIC-PrСГCrC,PSC-. P' PsCҗPiP°PSC-P·PjC- P»CҗPrPёPSPё P±C-P»P°СГC,PёPS PSPµ PjPµC,P°P±PsP»C-P·CrC" C,CҗCГCII. P PµP·CrP»CҗC,P°C,Pё PrPsСГP»C-PrP¶PµPSPSCII, PI CII PµPsPjCr P±CҗP°P»Pё CrC±P°СГC,Cҗ PIP°C+C-C"PSC,Pё P· PİPsCҗCrCёPµPSPSCII Pj C,,CrPSPeC+C-C— PSPёCҗPsPe, PİPsPeP°P·P°P»Pё, C%Ps P±C-P»P°СГC,PёPS PiPsP»PsPIPSPёPj C±PёPSPsPj PIPёPIPsPrPёC,CҗCГCII PSPёCҗPeP°PjPё, P° P· P¶PsPIC±Cҗ, PIC-CҗPsPiC-PrPSPs, PIPёPIPsPrPёC,CҗCГCII P»PёCёPµ PSPµP·PSP°C±PSPsCҗ PjC-CҗPsCҗ. P—PjC-PSPё C,,CrPSPeC+C-C— PİPµC±C-PSPePё PSPµ PjP°CҗC,Cҗ PeP»C-PSC-C±PSPs P·PSP°C±CrC%PsPiPs PIPİP»PёPICr PSP° C,,P°СҗPjP°PePsPeC-PSPµC,PёPeCr P±C-P»P°СГC,PёPSCr.

PµP°C+C-C"PSC,Pё P»C-C.PSCHPsPiPs PIC-PeCr. P"°PSC- PіCҗPs

C,,P°СҗPjP°PePsPeC-PSPµC,PёPeCr PіCҗPµPİP°СҗP°C,Cr Cr PIP°C+C-C"PSC,C-PI PIC-PePsPj PİPsPSP°Pr 65 CҗPsPeC-PI PsP±PjPµP¶PµPSC-. PαP°СҗPjP°PePsPeC-PSPµC,PёC±PSC- PİP°СҗP°PjPµC,CҗPё P±C-P»P°СГC,PёPSCr Cr PIP°C+C-C"PSC,C-PI PIC-PePsPj PİPsPSP°Pr 65 CҗPsPeC-PI C- Cr PIP°C+C-C"PSC,C-PI 18Bҗ"35 CҗPsPeC-PI СГC,P°C,PёСГC,PёC±PSPs P·PSP°C±CrC%Pµ PSPµ PIC-PrCҗC-P·PSCII CҗC,CҗCГCII.

P"°C-C,Pё. P"°PSC- P· C,,P°СҗPjP°PePsPeC-PSPµC,PёPePё Cr PіC-PrP»C-C,PeC-PI (12Bҗ"17

CҗPsPeC-PI) PIC-PrСГCrC,PSC-, PsСГPeC-P»CҗPePё PrP»CII C±CҗPsPiPs P»C-PeP°СҗCГCҗPePsPiPs P·P°СГPsP±Cr PIPIP°P¶P°C" C,CҗCГCII PrPsCҗPµC±PSPsCҗ PµPeСГC,CҗP°PİPsP»CII C+C-CII PrP°PSPёC..., PsC,CҗPёPjP°PSPёC... Cr PrPsCҗPsСГP»PёC....

РҗP»C-PSC-C±PSC- C...P°СҗP°PeC,PµСҗPёCГC,PёPePё.

PµPsPeP°P·P°PSPSCII.

P"°P»CII СГPёPjPіC,PsPjP°C,PёC±PSPsPiPs P»C-PeCrPIP°PSPSCII P°P»PµСҗPiC-C±PSPsPiPs CҗPёPSPsPePsPSBҗ™ CҗPSPeC,PёPIC-C,Cr (СГPµP·PsPSPSPsPiPs C,P°

C†C-P»PsCḡC-C†PSPsPiPs) C- PeCḡPsPiPëPIBḡ™ CḡPSPePë.

PμCḡPsC,PëPiPsPeP°P·P°PSPSCḡ.

PμC-PrPIPëC%oPμPSP° C†C†C,P»PëPIC-CḡC,CH PrPs PrC-CḡC†PsC— CḡPμC†PsPIPëPSPë P°P±Ps PrPs P±C†PrCH-CḡPePsC— P· PrPsPiPsPjC-PḡPSPëC... CḡPμC†PsPIPëPS.

P'P·P°C" PjPsPrC-Cḡ P· C-PSC€PëPjPë P»C-PeP°CḡCḡCHPePëPjPë P·P°CḡPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PNë.

P'P·P°C" PjPsPrC-Cḡ P· C—PḡPμCḡ. P†PḡP° P·PSPëPḡC†C" PSP° 30 %
P±C-PsPrPsCḡC,C†PiPSC-CḡC,CH P±C-P»P°CḡC,PëPSC†, PiCḡPëPNëPSCḡC,PsPiPs PICḡPμCḡPμPrPëPSC†.

P'P·P°C" PjPsPrC-Cḡ P· PiCḡPμPNëPiC,,CḡC†C,PsPIPëPj CḡPsPePsPj. Pj CḡP°P·C- PsPrPSPsC†P°CḡPSPsPiPs PiCḡPëPNëPsPjC† P±C-P»P°CḡC,PëPSC† PI PrPsP·C- 20 PjPi C- PiCḡPμPNëPiC,,CḡC†C,PsPIPsPiPs CḡPsPeC† P±C-PsPrPsCḡC,C†PiPSC-CḡC,CH P±C-P»P°CḡC,PëPSC† P·PSPëPḡC†PIP°P»P°CḡCḡ PSP° 30 %. PμPsPrC-P±PSPëPNë PμC,,PμPeC, PjPsPḡPμ C,P°PePsPḡ CḡPiPsCḡC,PμCḡC-PiP°C,PëCḡCḡ PNë C† CḡP°P·C- P·P°CḡC,PsCḡC†PIP°PSPSCḡ C-PSC€PëC... C,,CḡC†PeC,PsPIPëC... CḡPsPeC-PI. PḡC,C†PiC-PSCH P·PjPμPSC€PμPSPSCḡ P±C-PsPrPsCḡC,C†PiPSPsCḡC,C- PjPsPḡPμ CḡC-P·PSPëC,PëCḡCḡ P·P°P»PμPḡPSPs PIC-Pr PIPëCḡPsP±PSPëPeP° CḡPsPeC† C,P° C,,CḡC†PeC,C-PI. PḡPμC...P°PSC-P·Pj C†C-C" C— PIP·P°C" PjPsPrC-C— PiPsP»CḡPiP°C" C† PiCḡPëPiPSC-C†PμPSPSC- P±C-P»PeP°-PiPμCḡPμPSPsCḡPSPëPeP° OATP1A2, PrP»Cḡ CḡPePsPiPs P±C-P»P°CḡC,PëPS C" CḡC†P±CḡC,CḡP°C,PsPj (PrPëPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°B»). P>C-PeP°CḡCḡCHPeC- P·P°CḡPsP±Pë, C%oPs C" CḡC†P±CḡC,CḡP°C,P°PjPë P°P±Ps C-PSPiC-P±C-C,PsCḡP°PjPë OATP1A2, C,P°PeC- CḡPe CḡPëC,PsPSP°PIC-Cḡ P°P±Ps CḡPëC,,P°PjPiC-C†PëPS, C,P°PePsPḡ PjPsPḡC†C,CH P·PjPμPSC€C†PIP°C,Pë PePsPSC†PμPSC,CḡP°C†C-Cḡ P±C-P»P°CḡC,PëPSC† PI PiP»P°P·PjC-.

P'P·P°C" PjPsPrC-Cḡ P· PePμC,PsPePsPSP°P·PsP»PsPj P°P±Ps PμCḡPëC,CḡPsPjC-C†PëPSPsPj. Pj CḡP°P·C- PsPrPSPsC†P°CḡPSPsPiPs PiCḡPëPNëPsPjC† P±C-P»P°CḡC,PëPSC† C- PePμC,PsPePsPSP°P·PsP»C† P°P±Ps PμCḡPëC,CḡPsPjC-C†PëPSC† AUC P±C-P»P°CḡC,PëPSC† P·P±C-P»CHC€C†PIP°P»P°CḡCḡ PIPrPIC-C†C-, P° Cmax Bḡ" C† 2Bḡ"3 CḡP°P·Pë. PμPsPrC-P±PSC- P·PjC-PSPë PjPsPḡPSP° PiPsCḡCḡPSPëC,Pë PIP·P°C" PjPsPrC-C" Cḡ PSP° CḡC-PIPSC- P±C-P»PeC-PI-PiPμCḡPμPSPsCḡPSPëPeC-PI, C%oPs PIC-PrPiPsPIC-PrP°CḡC,CH P·P° PIPëPIPμPrPμPSPSCḡ P»C-PeP°CḡCḡCHPePëC... P·P°CḡPsP±C-PI C-P· PeP»C-C,PëPS PePëC€PμC†PSPëPeC†, PsCḡPeC-P»CHPePë P±C-P»P°CḡC,PëPS C" CḡC†P±CḡC,CḡP°C,PsPj PrP»Cḡ P-PiP»C-PePsPiCḡPsC,PμC—PSC† C- PSPμ PjPμC,P°P±PsP»C-P·C†C" C,CHCḡCḡ (PrPëPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°B»). PkP° PiCḡPsC,,C-P»CH P±PμP·PiPμPePë P±C-P»P°CḡC,PëPSC†, P· PsPrPSPsPiPs P±PsPeC†, C,P° PePμC,PsPePsPSP°P·PsP»C† P°P±Ps PμCḡPëC,CḡPsPjC-C†PëPSC†, P· C-PSC€PsPiPs, C†C- P·PjC-PSPë, PNëPjPsPIC-CḡPSPs, PSPμ PIPiP»PëPIP°CḡC,CH. P†PSC€C- P»C-PeP°CḡCḡCHPeC- P·P°CḡPsP±Pë, C%oPs C" CḡC†P±CḡC,CḡP°C,P°PjPë P°P±Ps C-PSPiC-P±C-C,PsCḡP°PjPë P-gp, C,P°PeC- CḡPe C†PëPeP»PsCḡPiPsCḡPëPS, C,P°PePsPḡ PjPsPḡC†C,CH P·P±C-P»CHC€C†PIP°C,Pë PePsPSC†PμPSC,CḡP°C†C-Cḡ P±C-P»P°CḡC,PëPSC† PI PiP»P°P·PjC-.

P'P·P°C" PjPsPrC-Cḡ P· PrPëP»C,C-P°P·PμPjPsPj. Pj CḡP°P·C- PsPrPSPsC†P°CḡPSPsPiPs

PiC7P6PN6PsPjC7 20 PjPi P±C-P»P°C7C,P6PSC7 C- 60 PjPi PrP6P»C,C-P°P·PμPjC7 C_{max}
P±C-P»P°C7C,P6PSC7 P·P±C-P»CHC€C7PIP°P»P°C7C7 PSP° 50 %. PμPsPrC-P±PSP6PN6
PμC,,PμPeC, PjPsP¶PSP° PiPsC7C7PSP6C,P6 PIP·P°C”PjPsPrC-C”C7 PSP° C7C-PIPSC-
P±C-P»PeC-PI-PiPμC7PμPSPsC7PSP6PeC-PI (PrP6PI. C7PsP·PrC-P»
B«PαP°C7PjP°PePsPeC-PSPμC,P6PeP°B»), C%Ps PIC-PrPiPsPIC-PrP°C7C,C7 P·P°
PIP6PIPμPrPμPSPSC7 P»C-PeP°C7C7C7PeP6C... PiC7PμPiP°C7P°C,C-PI C-P·
PeP»C-C,P6PS PeP6C€PμC7PSP6PeC7; PSP° PiC7PsC,,C-P»C7 P±PμP·PiPμPeP6
P±C-P»P°C7C,P6PSC7 C7PμPN6 PμC,,PμPeC,, PN6PjPsPIC-C7PSPs, PSPμ PIPiP»P6PIP°C”.

P’P·P°C”PjPsPrC-C7 P· PμC,P6P»PsPIP6Pj C7PiP6C7C,PsPj. PμC-C7P»C7
PsPrPSPsC7P°C7PSPsPiPs P·P°C7C,PsC7C7PIP°PSPSC7 P°P»PePsPiPsP»C7 C-
P±C-P»P°C7C,P6PSC7 PI PrPsP·C- 20 PjPi PiC7P6C...PsPjPsC,PSC7PSC- C,,C7PSPeC7C-C—
P·PSP°C...PsPrP6P»P6C7C7 PSP° C,PSPjC7 P¶ C7C-PIPSC-, C%Ps PN6 PiC-C7P»C7
PsPrPSPsC7P°C7PSPsPiPs P·P°C7C,PSC7C7PIP°PSPSC7 P°P»PePsPiPsP»C7 C-
PiP»P°C7PμP±Ps.

P’P·P°C”PjPsPrC-C7 P· P»PsC7P°P·PμPiP°PjPsPj. Pj C7P°P·C- P·P°C7C,PSC7C7PIP°PSPSC7
P±C-P»P°C7C,P6PSC7 C7 PrPsP·C- 20 PjPi PsPrPSPsC7P°C7PSPs P·
P»PsC7P°P·PμPiP°PjPsPj C7 PrPsP·C- 3 PjPi C7PiC7PsPrPsPIP¶ 8 PrPSC-PI
PiPsC7P6P»PμPSPSC7 PiC7P6PiPSC-C7C7PIP°P»C7PSPsC— PrC-C—
P»PsC7P°P·PμPiP°PjC7 PSP° P7P6P7 PIP6C7PIP»PμPSPs PSPμ P±C7P»Ps.

P”C-C,P6. P”PsC7P»C-PrP¶PμPSPSC7 PIP·P°C”PjPsPrC-C— P· C-PSC€P6PjP6
P»C-PeP°C7C7C7PeP6PjP6 P·P°C7PsP±P°PjP6 PiC7PsPiPsPrP6P»P6C7C7 C,C-P»C7PeP6 C7
PrPsC7PsC7P»P6C.... P6C7C-PeC7C”C,C7C7C7, C%Ps C7C,C7PiC-PSC7 PIP·P°C”PjPsPrC-C— P·
C-PSC€P6PjP6 P»C-PeP°C7C7C7PeP6PjP6 P·P°C7PsP±P°PjP6 C,P° C-PSC€C- C,,PSC7PjP6
PIP·P°C”PjPsPrC-C— P±C7PrC7C,C7 PiPsPrC-P±PSP6PjP6 C7 PrC-C,PμPN6 PIC-PePsPj PIC-Pr 12
PrPs 17 C7PsPeC-PI.

P6C7PsP±P»P6PIP6C7C- P·P°C7C,PSC7C7PIP°PSPSC7.

Pj PiP°C7C-C”PSC,C-PI P· PiPsPjC-C7PSP6Pj P°P±Ps C,C7P¶PeP6Pj PiPsC7C7C€PμPSPSC7Pj
C,,C7PSPeC7C-C— PSP6C7PsPe PsPrPSPsC7P°C7PSPμ P·P°C7C,PSC7C7PIP°PSPSC7
P±C-P»P°C7C,P6PSC7 P· C-PSPiC-P±C-C,PSC7P°PjP6 P-PiP»C-PePsPiC7PsC,PμC—PSC7
(PePμC,PSPePsPSP°P·PsP», PμC7P6C,C7PsPjC-C7P6PS, C7P6PeP»PsC7PiPsC7P6PS,
C7P6C,PSPSP°PIC-C7, PrP6P»C,C-P°P·PμPj C,PSC%Ps) PjPsP¶Pμ PiC7P6P·PiPsPrP6C,P6 PrPs
PiC-PrPIP6C%PμPSPSC7 C7C-PIPSC7 P±C-P»P°C7C,P6PSC7 PI PiP»P°P·PjC- PeC7PsPIC-,
P·P±C-P»C7C€C7C7C7P6 C7P6P·P6Pe PN6PsPiPs PiPsP±C-C7PSP6C... C7PμP°PeC7C-PN6.
P7PsPjC7 PiP°C7C-C”PSC,P°Pj C-P· C7PμC7PμPrPSC-Pj P°P±Ps C,C7P¶PeP6Pj
PiPsC7C7C€PμPSPSC7Pj C,,C7PSPeC7C-C— PSP6C7PsPe C7P»C-Pr C7PSP6PeP°C,P6
PsPrPSPsC7P°C7PSPsPiPs P·P°C7C,PSC7C7PIP°PSPSC7 P±C-P»P°C7C,P6PSC7 C,P°
C-PSPiC-P±C-C,PSC7C-PI P-PiP»C-PePsPiC7PsC,PμC—PSC7.

PμPsPIC-PrPsPjP»C7P»PsC7C7 PiC7Ps PIP6PiP°PrPeP6 PiPsPrPsPIP¶PμPSPSC7
C-PSC,PμC7PIP°P»C7 QT PSP° PμP»PμPeC,C7PsPeP°C7PrC-PsPiC7P°PjC- C7

PiP°C†C-C" PSC,C-PI, CΠPeC- P·P°C†C,PsC†PsPIC†PIP°P»Pë P±C-P»P°C†C,PëPS (PrPëPI.
C†PpP·PrC-P»Pë B«PμPsP±C-C†PSC- C†PμP°PeC†C-C-B», B«PμPμC†PμPrPsP·C†PIP°PSPSCΠB»
C,P° B«PαP°C†PjP°PePsP»PsPiC-C†PSC- PIP»P°C†C,PëPIPSc†C,C-B»). P>C-PeP°C†C†C†PeC-
P·P°C†PsP±Pë, CΠPeC- C†PiC†PëC†PëPSCΠC†C,C† PiPsPrPsPIP°PμPSPSCΠ QT/QTc,
PiC†PëPiC†C†C,PëPjPs P·P±C-P»C†C€C†C†C,C† C†PëP·PëPe PiC-C†C†PμC,PSPSc—
C€P»C†PSPSc†PePsPIPsC— C,P°C...C-PeP°C†PjC-C—.

PÿPsPjC† C†P»C-Pr P· PsP±PμC†PμP°PSC-C†C,C† PiC†PëP·PSP°C†P°C,Pë P±C-P»P°C†C,PëPS
PiP°C†C-C" PSC,P°Pj, C† CΠPePëC... PiC-PrPIPëC%PμPSPëP№ C†PëP·PëPe
PiPsPrPsPIP°PμPSPSCΠ C-PSC,PμC†PIP°P»C† QT/QTc. PjPμ C†C,PsC†C†C" C,C†C†CΠ
PiP°C†C-C" PSC,C-PI C-P· C†PμC†C†PμPIPëPjPë P°C†PëC,PjC-CΠPjPë PI P°PSP°PjPSPμP·C-;
PiP°C†C-C" PSC,C-PI P· PiC-PiPsPeP°P»C-C" PjC-C" C†, PiC-PiPsPjP°PiPSC-C" PjC-C" C†,
PiC-PiPsPeP°P»C†C†C-C" PjC-C" C†; PiP°C†C-C" PSC,C-PI P· PiC-PrC,PIPμC†PjPrP°PμPSPëPj
PiPsPrPsPIP°PμPSPSCΠPj C-PSC,PμC†PIP°P»C† QT P°P±Ps P·PSP°C†PSPSc†
P±C†P°PrPëPeP°C†PjC-C" C†; PiP°C†C-C" PSC,C-PI, CΠPeC- PsPrPSPSc†P°C†PSPs
P·P°C†C,PsC†PsPIC†C†C,C† C-PSC€C- P»C-PeP°C†C†C†PeC- P·P°C†PsP±Pë,
PiPsPiB†™ CΠP·P°PSC- P· PiPsPrPsPIP°PμPSPSCΠPj QT/QTc.

*P—P°C†C,PsC†C†PIP°PSPSCΠ C† PiPμC†C-PsPr PIP°PiC-C,PSPSc†C,C- P°P±Ps
PiPsPrC†PIP°PSPSCΠ PiC†C†PrPrC†.*

*P'P°PiC-C,PSC-C†C,C†. P"°PSC- C%PsPrPs P·P°C†C,PsC†C†PIP°PSPSCΠ
P±C-P»P°C†C,PëPSC† PIP°PiC-C,PSPëPj P°C-PSPeP°Pj PIC-PrC†C†C,PSC- P°P±Ps
PsP±PjPμP°PμPSC-.*

P"PsC†P»C-PrP°PμPSPSCΠ PSP° C,PIP°C†PëPSP°C... PSPμ PIPëCΠPIPëP»Pë PiC†CΠPjPsPiPs
P°P±Ps PSPμPiC†CΠPjPsPiPs C€PeC-PrP»PëPIPsPiPs PIPiP»PëPIC† PSP°
C†PμPiC†PpPrC†PeC,PëPIPSC† C,,C†PSPeC†C-C†, PiPsP»PsPiPë P°P±Ps
PiPsC†C,PSP°C,P°P»C†PSPëP№ C†PpP·PIPëC,PsPe. P— PjC-C†PeC†PIP°PSC† P±PμP·PiPμPePë
P±P°P°PSPs C†PSPëPeP°C,Pë PiC†PëP№PsPjC† P»C-PeP°C†C†C†PePsPiPs P·P°C†PsP±C†
P' C-P»P°PiC-C†^{B®} PiC-Pr C†P°C† PIP°PiC-C,PSPSc†C,C-.

*P"PsPrC†PIP°PSPSCΠ PiC†C†PrPrC†. P"PsC†P»C-PrP°PμPSPSCΠ C%PsPrPs
PIPëPrC-P»PμPSPSCΠ P±C-P»P°C†C,PëPSC† PI PiC†C†PrPSPμ PjPsP»PsPePs
P»C†PrPëPSPë PSPμ PiC†PpPrPsPrPëP»PëC†C†. PkP°C†PIPSC-
C,,P°C†PjP°PePsPeC-PSPμC,PëC†PSC- PrP°PSC- PiPsPeP°P·P°P»Pë, C%Ps C†
C,PIP°C†PëPS P±C-P»P°C†C,PëPS PiC†PpPSPëPeP°C" PI PiC†C†PrPSPμ PjPsP»PsPePs.
P C-C€PμPSPSCΠ PiC†Pp PiC†PpPrPsPIP°PμPSPSCΠ/PiC†PëPiPëPSPμPSPSCΠ
PiPsPrC†PIP°PSPSCΠ PiC†C†PrPrC† P°P±Ps
PiC†PëPiPëPSPμPSPSCΠ/C†C,C†PëPjP°PSPSCΠ PIC-Pr C,PμC†P°PiC-C—
P»C-PeP°C†C†C†PePëPj P·P°C†PsP±PsPj P' C-P»P°PiC-C†^{B®} PSPμPsP±C...C-PrPSPs
PiC†PëP№PjP°C,Pë, P±PμC†C†Pë PrPs C†PIP°PiPë PePsC†PëC†C,C†
PiC†C†PrPSPsPiPs PIPëPiPsPrPsPIC†PIP°PSPSCΠ PrP»C† PrPëC,PëPSPë C-
PePsC†PëC†C,C† C,PμC†P°PiC-C— P±C-P»P°C†C,PëPSPsPj PrP»C† PjP°C,PμC†C-.*

*PαPμC†C,PëP»C†PSC-C†C,C†. PλP»C-PSC-C†PSC- PrP°PSC- PsP±PjPμP°PμPSC- P°P±Ps
PIC-PrC†C†C,PSC-. P"PsC†P»C-PrP°PμPSPSCΠ PSP° C%C†C†P°C... PSPμ PIPëCΠPIPëP»Ps
P°PpPrPSPsPiPs PSPμPiP°C,PëPIPSPsPiPs PIPiP»PëPIC† PSP° C,,PμC†C,PëP»C†PSC-C†C,C†.*

P—PrP°C,PSC—CÍC,CH PIPiP»PëPIP°C,Pë PSP° C€PIPëPrPeC—CÍC,CH CŤPµP°PeC†C— PiCŤPë PePµCŤCáPIP°PSPSC— P°PIC,PsC,CŤP°PSCÍPiPsCŤC,PsPj P°P±Ps C—PSC€PëPjPë PjPµC...P°PSC—P·PjP°PjPë.

P°PSCÍP»C—PrP¶PµPSPSCŤ PIPiP»PëPICr P±C—P»P°CÍC,PëPSCr PSP° P·PrP°C,PSC—CÍC,CH PePµCŤCáPIP°C,Pë P°PIC,PsC,CŤP°PSCÍPiPsCŤC,PsPj PiCŤPµPrPµPjPsPSCÍC,CŤCáPIP°P»Ps, C%Ps Cr PrPsCŤPsCÍP»PëC... P»C—PeCÍPIP°PSPSCŤ P±C—P»P°CÍC,PëPSPsPj Cr PrPsP·C— 20 PjPi PSPµ PIPiP»PëPIP°P»Ps PSP° P·PrP°C,PSC—CÍC,CH PePµCŤCáPIP°C,Pë C,CŤP°PSCÍPiPsCŤC,PSPëPjPë P·P°CÍPsP±P°PjPë. PhPrPSP°Pe PiP°C†C—C°PSC,C—PI CÍP»C—Pr C—PSC,,PsCŤPjCáPIP°C,Pë PiCŤPµ C,Pµ, C%Ps PI PsPeCŤPµPjPëC... PIPëPiP°PrPeP°C... PiCŤPµPiP°CŤP°C, PjPsP¶Pµ PIPëPeP»PëPeP°C,Pë CÍPsPSP»PëPIC—CÍC,CH C—, C,P°PePëPj C†PëPSPsPj, PIPiP»PëPIP°C,Pë PSP° P·PrP°C,PSC—CÍC,CH PePµCŤCáPIP°C,Pë P°PIC,PsC,CŤP°PSCÍPiPsCŤC,PsPj P°P±Ps PiCŤP°C†CŤPIP°C,Pë P· C—PSC€PëPjPë PjPµC...P°PSC—P·PjP°PjPë.

PŸPiPsCÍC—P± P·P°CÍC,PsCÍCáPIP°PSPSCŤ C,P° PrPsP·Pë.

P°PsP·CáPIP°PSPSCŤ.

P°PsCŤPsCÍP»C— C,P° PrC—C,Pë (PIC—PePsPj PIC—Pr 12 CŤPsPeC—PI). 20 PjPi P±C—P»P°CÍC,PëPSCr (1 C,P°P±P»PµC,PeP°) 1 CŤP°P· PSP° PrPsP±Cá PrP»CŤ PíPsP»PµPiC€PµPSPSCŤ CÍPëPjPiC,PsPjC—PI P°P»PµCŤPiC—C†PSPsPiPs CŤPëPSPsPePsPSBŤ™ CŤPSPeC,PëPIC—C,Cr (CÍPµP·PsPSPSPsPiPs C— C†C—P»PsCŤC—C†PSPsPiPs) C,P° PeCŤPsPiPëPiBŤ™ CŤPSPePë.

PŸP°P±P»PµC,PeCá CÍP»C—Pr PiCŤPëPNëPjP°C,Pë P·P° 1 PiPsPrPëPSCr PrPs P°P±Ps C†PµCŤPµP· 2 PiPsPrPëPSPë PiC—CÍP»CŤ PiCŤPëPNëPsPjCá C—P¶C— P°P±Ps C,,CŤCáPeC,PsPiPsPiPs CÍPsPeCá (PrPëPI. CŤPsP·PrC—P» B«P·P·P°C°PjPsPrC—CŤ P· C—PSC€PëPjPë P»C—PeP°CŤCÍCHPePëPjPë P·P°CÍPsP±P°PjPë C,P° C—PSC€C— PIPëPrPë PIP·P°C°PjPsPrC—PNëB»).

PhCÍPsP±P»PëPIC— PiCŤCáPiPë PiP°C†C—C°PSC,C—PI.

PµP°C†C—C°PSC,Pë P»C—C,PSCHPsPiPs PIC—PeCá. PµP°C†C—C°PSC,P°Pj P»C—C,PSCHPsPiPs PIC—PeCá PePsCŤPëPiCáPIP°C,Pë PrPsP·Cá PSPµ PiPsC,CŤC—P±PSPs (PrPëPI. CŤPsP·PrC—P» B«PαP°CŤPjP°PePsPrPëPSP°PjC—PeP°B» C,P° B«PαP°CŤPjP°PePsPeC—PSPµC,PëPeP°B»).

PµCŤPë PiPsCŤCáC€PµPSPSC— C,,CáPSPeC†C—C— PSPëCŤPsPe. PµP°C†C—C°PSC,P°Pj P· PiPsCŤCáC€PµPSPSCŤPjPë C,,CáPSPeC†C—C— PSPëCŤPsPe PePsCŤPëPiCáPIP°C,Pë PrPsP·Cá PSPµ PiPsC,CŤC—P±PSPs (PrPëPI. CŤPsP·PrC—P» B«PαP°CŤPjP°PePsPeC—PSPµC,PëPeP°B»).

PµCŤPë PiPsCŤCáC€PµPSPSCŤC... C,,CáPSPeC†C—C— PiPµC†C—PSPePë. P°PSCÍPIC—Pr PeP»C—PSC—C†PSPsPiPs P·P°CÍC,PsCÍCáPIP°PSPSCŤ PiCŤPµPiP°CŤP°C,Cá PiP°C†C—C°PSC,P°Pj P· PiPsCŤCáC€PµPSPSCŤPjPë C,,CáPSPeC†C—C— PiPµC†C—PSPePë PIC—PrCÍCáC,PSC—PNë. PhCÍPeC—P»CHPePë P±C—P»P°CÍC,PëPSPµ PiC—PrPrP°C°C,CHCÍCŤ PjPµC,P°P±PsP»C—P·PjCá C,P° PIPëPiPsPrPëC,CHCÍCŤ PiPsP»PsPiPSPëPj C†PëPSPsPj PSPëCŤPeP°PjPë, PiPsCŤCáC€PµPSPSCŤ C,,CáPSPeC†C—C— PiPµC†C—PSPePë PSPµ PiPsPiPëPSPSPs PiCŤPëP·PiPsPrPëC,Pë PrPs P·P±C—P»CHC€PµPSPSCŤ PNëPsPiPs CÍPëCÍC,PµPjPSPsC— PrC—C—

PrPs PSPμP±PμP·PīPμC±PSPsPiPs CḡC-PIPSCḡ. PŷPsPjCř PīP°C†C-C" PSC,P°Pj P·
PīPsCḡCřCεPμPSPSCḡPjPë C,,CřPSPeC†C-C— PīPμC±C-PSPePë PePsCḡPëPīCřPIP°C,Pë PrPsP·Cř
PSPμ PīPsC,CḡC-P±PSPs (PrPëPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°B»).

P" C-C,Pë. P—P°C†C,PsC†PsPICřPIP°C,Pë P±C-P»P°C†C,PëPS PīCḡPë P°P»PμCḡPiC-C±PSPsPjCř
CḡPëPSPsPePsPSBḡ™ CḡPSPeC,PëPIC-C,C- C,P° PeCḡPsPīPëPIBḡ™ CḡPSC†C- PrC-C,CḡPj
PIC-PePsPj PIC-Pr 0 PrPs 2 CḡPsPeC-PI PSPμPrPsC†C-P»CḡPSPs. P'PμP·PīPμPeP° C-
PμC,,PμPeC,PëPIPSC-C†C,Cḡ P·P°C†C,PsC†CřPIP°PSPSCḡ PrC-C,CḡPj PIC-PePsPj PrPs 12
CḡPsPeC-PI PSP° C†CḡPsPiPsPrPSC- PSPμ PIC†C,P°PSPsPIP»PμPSC-.

PŷCḡPëPIP°P»C-C†C,Cḡ P»C-PeCžPIP°PSPSCḡ.B PμP°C†C-C" PSC,P°Pj P·
P°P»PμCḡPiC-C±PSPëPj CḡPëPSC-C,PsPj P»C-PeP°CḡC†CḡPePëPñ P·P°C†C-P± C†P»C-Pr
P·P°C†C,PsC†PsPICřPIP°C,Pë C,C-P»CḡPePë PI PīPμCḡC-PsPr PePsPSC,P°PeC,Cř P·
P°P»PμCḡPiPμPSP°PjPë. PμP°C†C-C" PSC,P°Pj C-P· C†PμP·PsPSPSPëPj P°P»PμCḡPiC-C±PSPëPj
CḡPëPSC-C,PsPj P»C-PeCřPIP°PSPSCḡ PjPsP¶PSP° PīCḡPëPīPëPSPëC,Pë PīC-C†P»Cḡ
PīPsPjBḡ™ CḡPeCεPμPSPSCḡ C†PëPjPīC,PsPjC-PI C,P° PīPsPSPsPIPëC,Pë PīC-C†P»Cḡ C—C...
PīPsPIPμCḡPSPμPSPSCḡ. PμP°C†C-C" PSC,P°Pj P· C†C-P»PsCḡC-C±PSPëPj
P°P»PμCḡPiC-C±PSPëPj CḡPëPSC-C,PsPj PīCḡPμPīP°CḡP°C, PjPsP¶PSP°
P±PμP·PīPμCḡPμCḡPIPSPs P·P°C†C,PsC†PsPICřPIP°C,Pë PIPīCḡPsPrPsPIP¶ PīPμCḡC-PsPrCř
PePsPSC,P°PeC,Cř P· P°P»PμCḡPiPμPSP°PjPë. Pj PīP°C†C-C" PSC,C-PI P·
PeCḡPsPīPëPIBḡ™ CḡPSPePsCḡ C,CḡPëPIP°P»C-C†C,Cḡ P»C-PeCřPIP°PSPSCḡ
P·P°P»PμP¶PëC,Cḡ PIC-Pr C...P°CḡP°PeC,PμCḡCř C,P° C,CḡPëPIP°P»PsC†C,C-
C†PëPjPīC,PsPjC-PI, P° C,P°PePsP¶ PIC-Pr C—C... PrPëPSP°PjC-PePë.

PŷPīPsC†C-P± P·P°C†C,PsC†CžPIP°PSPSCḡ.

P" P»Cḡ PīPμCḡPsCḡP°P»CḡPSPsPiPs P·P°C†C,PsC†CřPIP°PSPSCḡ.

PŷP°P±P»PμC,PePë C†P»C-Pr P·P°PīPëPIP°C,Pë PIPsPrPsCḡ. P"PsP±PsPICř PrPsP·Cř
CḡPμPePsPjPμPSPPrCřC" C,CḡC†Cḡ PīCḡPëPñPjP°C,Pë P·P° PsPrPëPS PīCḡPëPñPsPj.

P" C-C,Pë.

P'PμP·PīPμPeP° C,P° PμC,,PμPeC,PëPIPSC-C†C,Cḡ P±C-P»P°C†C,PëPSCř PrP»Cḡ PrC-C,PμPñ
PIC-PePsPj PrPs 12 CḡPsPeC-PI PSPμ PīC-PrC,PIPμCḡPrP¶PμPSC-.

PμPμCḡPμPrPsP·CžPIP°PSPSCḡ.

P†PSC,,PsCḡPjP°C†C-Cḡ C†C,PsC†PsPIPSPs PiPsC†C,CḡPsPiPs PīPμCḡPμPrPsP·CřPIP°PSPSCḡ
P±C-P»P°C†C,PëPSPsPj P±CřP»P° PsC,CḡPëPjP°PSP° PI C...PsPrC- PeP»C-PSC-C±PSPëC...
PIPëPīCḡPsP±CřPIP°PSCḡ, PīCḡPsPIPμPrPμPSPëC... PīC-Pr C±P°C† CḡPsP·CḡPsP±PePë C,P°
PīPsC†C,PjP°CḡPePμC,PëPSPiPsPiPsPiPs C†PīPsC†C,PμCḡPμP¶PμPSPSCḡ. Pj
PeP»C-PSC-C±PSPëC... PrPsC†P»C-PrP¶PμPSPSCḡC... PīC-C†P»Cḡ PīCḡPëP·PSP°C±PμPSPSCḡ
PrPsCḡPsC†P»PëPj P·PrPsCḡPsPIPëPj PrPsP±CḡPsPIPSP»CḡC†CḡPj P±C-P»P°C†C,PëPSCř PI
PrPsP·P°C..., C%Ps PīPμCḡPμPIPëC% CřPIP°P»Pë C,PμCḡP°PīPμPIC,PëC±PSCř PI 10Bḡ"11
CḡP°P·C-PI (220 PjPi Cř PIPëPīP»CḡPrC- PsPrPSPsCḡP°P·PsIPsC— PrPsP·Pë P°P±Ps 200 PjPi
PSP° PrPsP±Cř PīCḡPsC,CḡPiPsPj 7 PrPSC-PI), C±P°C†C,PsC,P° PIPëPSPëPePSPμPSPSCḡ

PiPsP±C-C±PSPëC... CḡPµP°PeC†C-PMᵇ P±C†P»P° PIPrPIC-C±C- PIPëC%PsCḡ, PSC-Pḡ PSP°
C,P»C- P·P°C†C,PsC†C†PIP°PSPSCḡ PiP»P°C†PµP±Ps. P°Ps PiPsP±C-C±PSPëC...
CḡPµP°PeC†C-PMᵇ, PiCḡPs CḡPeC- PSP°PMᵇC±P°C†C,C-C€Pµ PiPsPIC-PrPsPjP»CḡP»PsC†Cḡ,
PSP°P»PµPḡP°P»Pë P·P°PiP°PjPsCḡPsC±PµPSPSCḡ, PiPsP»PsPIPSPëPNᵇ P±C-P»Cḡ C-
PSC†PrPsC,P°. PµPsPIC-PrPsPjP»PµPSCḡ PiCḡPs C†PµCḡPMᵇPsP·PSC- PiPsP±C-C±PSC-
CḡPµP°PeC†C-C— C,P° P·PSP°C±PSPµ PiPsPrPsPIPḡPµPSPSCḡ C-PSC,PµCḡPIP°P»C† QTc PSPµ
P±C†P»Ps. P†PSC,,PsCḡPjP°C†C-Cḡ, P·C-P±CḡP°PSP° PiC-Pr C±P°C†
PiPsC†C,PjP°CḡPePµC,PëPSPiPsPiPsPiPs C†PiPsC†C,PµCḡPµPḡPµPSPSCḡ, PIC-PrPiPsPIC-PrP°C°
PrP°PSPëPj, PsC,CḡPëPjP°PSPëPj C†PiCḡPsPrPsPIPḡ PeP»C-PSC-C±PSPëC...
PIPëPiCḡPsP±C†PIP°PSCḡ.

Pj CḡPµC,PµP»CḡPSPsPjC† PiPµCḡPµC...CḡPµC†PSPsPjC† PrPsC†P»C-PrPḡPµPSPSC-
C-PSC,PµCḡPIP°P»C-PI QT/QTc P·P° C†C±P°C†C,Cḡ 30 P·PrPsCḡPsPIPëC... PrPsCḡPsC†P»PëC...
PrPsP±CḡPsPIPpsP»CḡC†C-PI PeCḡPëC,PëC±PSP° PsC†C-PSPeP° PIPiP»PëPIC†
P±P°PiP°C,PsCḡP°P·PsPiPsC— PrPsP·Pë P±C-P»P°C†C,PëPSC† (100 PjPi × 4 PrPSC-) PSP°
CḡPµPiPsP»CḡCḡPëP·P°C†C-Cḡ C€P»C†PSPsC±PeC-PI PSPµ PIPëCḡPIPëP»P° P·PSP°C±PSPsPiPs
PiPsPrPsPIPḡPµPSPSCḡ C-PSC,PµCḡPIP°P»C† QTc.

Pj CḡP°P·C- PiPµCḡPµPrPsP·C†PIP°PSPSCḡ CḡPµPePsPjPµPSPrC†C°C,CḡC†Cḡ
C†PëPjPiC,PsPjP°C,PëC±PSPµ C,P° PiC-PrC,CḡPëPjC†PIP°P»CḡPSPµ P»C-PeC†PIP°PSPSCḡ.

PŸPiPµC†PëC,,C-C±PSPëPNᵇ P°PSC,PëPrPsC, P±C-P»P°C†C,PëPSC† PSPµPIC-PrPsPjPëPNᵇ.

PµPsP±C-C±PSC- CḡPµP°PeC†C-C—.

Pj C...PsPrC-B PeP»C-PSC-C±PSPëC... PrPsC†P»C-PrPḡPµPSCḡ C† PiP°C†C-C°PSC,C-PI, CḡPeC-
C†C,CḡP°PḡPrP°P»Pë PIC-Pr P°P»PµCḡPiC-C±PSPsPiPs
CḡPëPSPsPePsPSḡḡ™ CḡPSPeC,PëPIC-C,C† P°P±Ps C...CḡPsPSC-C±PSPsC—
C-PrC-PsPiP°C,PëC±PSPsC— PeCḡPsPiPëPiḡḡ™ CḡPSPePë, PiPsP±C-C±PSC- CḡPµP°PeC†C-C—
PiCḡPë P·P°C†C,PsC†C†PIP°PSPSC- P±C-P»P°C†C,PëPSC† PI PrPsP·C- 20 PjPi PIPëPSPëPeP°P»Pë
PiCḡPëP±P»PëP·PSPs P· C,C-C°Cḡ Pḡ C±P°C†C,PsC,PsCḡ, C%Ps PNᵇ PiCḡPë
P·P°C†C,PsC†C†PIP°PSPSC- PiP»P°C†PµP±Ps (12,7 % C- 2,8 %). PḡP»C-PSC-C±PSC-
PIPëPiCḡPsP±C†PIP°PSPSCḡ II C- III C,,P°P·Pë, PiCḡPsPIPµPrPµPSC- PiC-Pr C±P°C†
PeP»C-PSC-C±PSPsC— CḡPsP·CḡPsP±PePë, PsC...PsPiP»CḡPIP°P»Pë 2525
PiP°C†C-C°PSC,C-PI, CḡPePëC... P»C-PeC†PIP°P»Pë CḡC-P·PSPëPjPë PrPsP·P°PjPë
P±C-P»P°C†C,PëPSC†, P· PSPëC... 1697 PsC,CḡPëPjC†PIP°P»Pë P±C-P»P°C†C,PëPS C†
PrPsP·C- 20 PjPi. Pj C†PëC... PrPsC†P»C-PrPḡPµPSPSCḡC... 1362 PiP°C†C-C°PSC,Pë
PsC,CḡPëPjC†PIP°P»Pë PiP»P°C†PµP±Ps. PµP°C†C-C°PSC,Pë, CḡPeC-
PsC,CḡPëPjC†PIP°P»Pë P±C-P»P°C†C,PëPS C† PrPsP·C- 20 PjPi P·P°
PiPsPeP°P·P°PSPSCḡPj P°P»PµCḡPiC-C±PSPëPNᵇ
CḡPëPSPsPePsPSḡḡ™ CḡPSPeC,PëPIC-C, C±Pë C...CḡPsPSC-C±PSP°
C-PrC-PsPiP°C,PëC±PSP° PeCḡPsPiPëPiḡḡ™ CḡPSPeP°, PSP°PMᵇC±P°C†C,C-C€Pµ
PiPsPIC-PrPsPjP»CḡP»Pë PiCḡPs C,P°PeC- PiPsP±C-C±PSC- CḡPµP°PeC†C-C—
PiPsP»PsPIPSPëPNᵇ P±C-P»Cḡ, C†PsPSP»PëPIC-C†C,Cḡ, P·P°PiP°PjPsCḡPsC±PµPSPSCḡ
C,P° PIC,PsPjP»CḡPIP°PSC-C†C,Cḡ. PjC- PiPsP±C-C±PSC- CḡPµP°PeC†C-C—
PIPëPSPëPeP°P»Pë P· C±P°C†C,PsC,PsCḡ, PiPsCḡC-PIPSCḡPSPSPsCḡ P·
C±P°C†C,PsC,PsCḡ CḡPsP·PIPëC,PeC† PiPsP±C-C±PSPëC... CḡPµP°PeC†C-PMᵇ C†
PiP°C†C-C°PSC,C-PI, CḡPeC- PsC,CḡPëPjC†PIP°P»Pë PiP»P°C†PµP±Ps.

Р'РёСҫPsP±PSPёРё. РҫРҫ В«РѡР°СҫРјР°РёВ», РЈРёСҫР°С—PSP°

(РІРёСҫPsP±PSPёС†С,РІРs Р· РїСҫPsРrСrРёС†С— in bulk С„С—СҫРјРё-РІРёСҫPsP±PSPёРёР° Р>Р°Р±PsСҫР°С,PsСҫС—PsСr РќPsСҫРјPsPS, Рҫ.Рҫ., Р†СrРїР°PSC—Cҫ).

РњС—СrС†РµР·PSP°С...PsРrР¶РµPSPSCҫ РІРёСҫPsP±PSPёРёР° С,Р° Р°РrСҫРµСrР° РјС—СrС†Cҫ РїСҫPsРІР°РrР¶РµPSPSCҫ Р№PsРiPs РrС—CҫP»СҫPSPsСrС,С-.

РЈРёСҫР°С—PSP°, 04080, Рј. РљРёС—РІ, РІСrР». РљРёСҫРёР»С—РІСrСҫРёР°, 74.